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CHAPTER 1

HYDROCYANATION OF ALKENES AND ALKYNES

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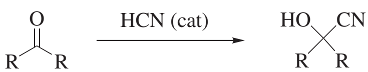
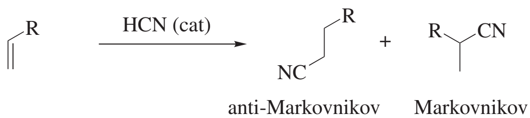
many talented scientists at DuPont, most notable among them Drs. Bill Drinkard, Chad Tolman, and Ron McKinney, who, during the course of developing the DuPont adiponitrile process, formulated many important concepts that helped define the role of ligands in homogeneous catalysis by organometallic complexes.

INTRODUCTION

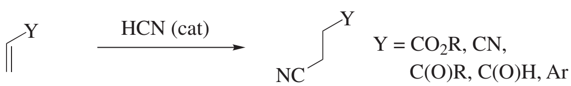
Hydrogen cyanide is an abundantly available feedstock that is useful for the synthesis of organonitrile intermediates which serve as precursors for amines, amides, isocyanates, carboxylic acids, and esters.[1] Many of these compounds are used in the manufacture of polymers, agrichemicals, cosmetics, and pharmaceuticals. Hydrogen cyanide itself is relatively unreactive, but in the presence of a catalyst HCN adds to carbonyl compounds, alkenes, and alkynes, offering a direct and economical way to such organonitrile intermediates (Eqs. 1–5).[2–6]



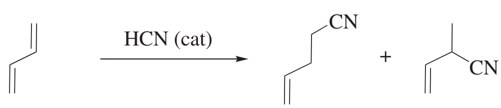
(Eq. 1)



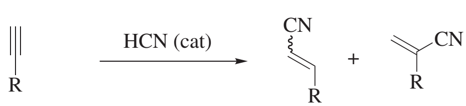
(Eq. 2)



(Eq. 3)



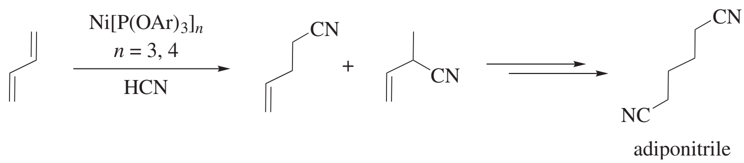
(Eq. 4)



(Eq. 5)

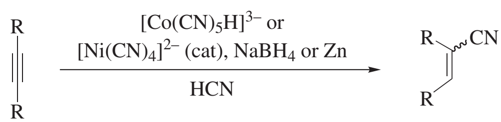
Hydrocyanation of activated substrates such as carbonyl compounds, imines, and electron-deficient alkenes (Eq. 3) usually occurs in the presence of a base, including cyanide ion itself.[7–9] Conjugate addition of HCN to α,β-unsaturated carbonyl compounds also proceed in the presence of Lewis acids such as alkylaluminum reagents (Nagata reaction),[10–12] aluminum salen complexes,[13] and gadolinium alkoxides.[14] Addition of HCN to an unactivated alkene or alkyne is best accomplished with a transition-metal-catalyst, usually a Ni or Pd complex. The classic example, which represents a very successful commercial application of this process, is DuPont's production of the nylon-66 precursor, adiponitrile, via hydrocyanation of 1,3-butadiene (Eq. 6).[15,16] This discovery sparked many seminal mechanistic investigations of transition-metal-catalyzed reactions.[17–23]

Concepts that emerged from these studies include the proposal that many catalytic processes proceed through coordinatively unsaturated 16-electron (or lower) intermediates,[24] and the importance of steric (e.g., ligand cone-angle θ) and electronic effects (e.g., Tolman χ-factor) on ligand substitution reactions.[20,22,25] Hydrocyanation of alkenes continues to offer opportunities for ligand/catalyst tuning to achieve higher efficiencies and selectivities at all levels in a key carbon–carbon bond-forming reaction.[26,27,27a]



(Eq. 6)

Until the late 1960s, the major industrial synthesis of acrylonitrile involved either the addition of HCN to acetylene at high temperature with no catalyst, or addition in the presence of a Cu(I)-catalyst at 80–90°.[1,3,7,28] Reactions involving low-valent Ni, Pd, and Co-complexes have since largely replaced these processes.[29,30] Zero-valent Ni arylphosphite complexes, and to a lesser extent, zero-valent palladium arylphosphine or arylphosphite complexes, catalyze addition of HCN to alkynes. On the basis of the initial discovery of the hydrocyanation of alkynes with stoichiometric $[Co(CN)_5H]^{3-}$, a new process using substoichiometric amounts of $Ni(CN)_4{}^{2-}$ and stoichiometric amounts of a reducing agent ($NaBH_4$ or Zn) has been reported for the addition of elements of HCN across an acetylene (Eq. 7).[31]



(Eq. 7)

This chapter focuses primarily on the metal-catalyzed hydrocyanation of alkenes and alkynes. Coverage of the catalyzed, conjugate addition of HCN to α, β-unsaturated carbonyl compounds will be limited to a brief mention of the results that appeared since the publication of the *Organic Reactions* chapter on the Nagata reaction.[10] Acetone cyanohydrin and trimethylsilyl cyanide (TMSCN), both commercially available reagents, can be used for the in situ generation of HCN. In some transition-metal-catalyzed additions, TMSCN acts as a surrogate for HCN, giving products where the TMS group replaces the hydrogen. Preparatively, these reagents provide some advantages since the handling of toxic HCN is avoided. Reactions of these reagents are included under the appropriate substrates, so that direct comparison of yield and selectivity can be made. Heterogeneous vapor-phase hydrocyanations catalyzed by metal oxides,[7,32–34] Lewis acids,[7] and transition metals,[32] and 1,2-additions of HCN to carbonyl compounds,[35] imines, or other related compounds[9] are not included here. Mowry's exhaustive review (1942)[7] should be consulted for early reports on the addition of alkali

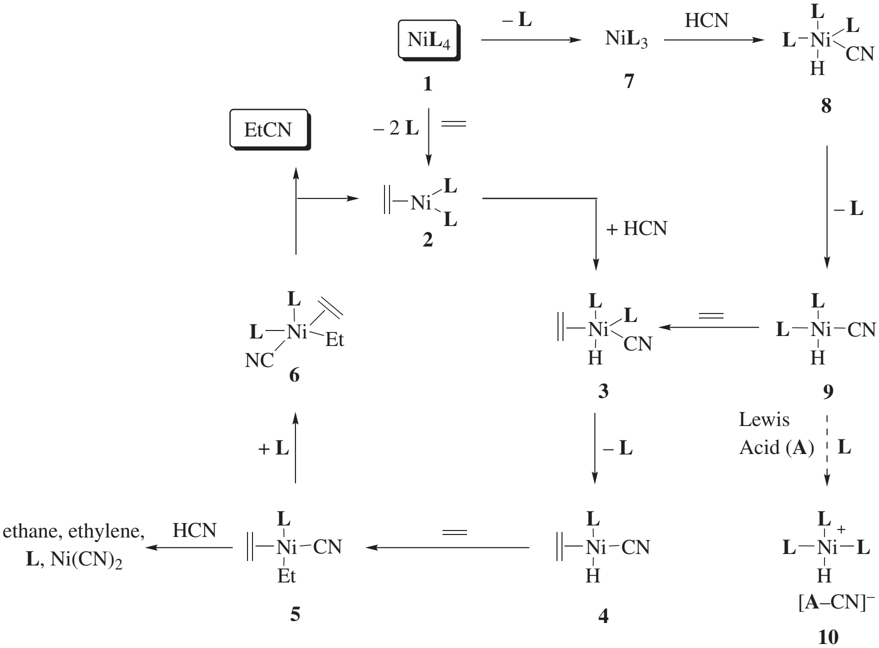
and alkaline earth metal salts to highly activated alkenes such as alkylidene malonates, cyanoacetates, and nitroalkenes. These reactions are often accompanied by side reactions, rearrangements of the primary products, and multiple additions. Because of the large commercial interest in hydrocyanation, many proprietary aspects of these reactions appear in the patent literature. Only the most relevant patents related to synthetic chemistry along with their *Chemical Abstracts* citations are mentioned in this article. This chapter covers the literature on hydrocyanation up to the end of 2008.

MECHANISM AND STEREOCHEMISTRY

Hydrocyanation of Alkenes

Mechanism. Some of the earliest work on homogeneous hydrocyanation of alkenes uses dicobalt octacarbonyl[36,37] and Cu(I)[38] salts as catalysts. For example, catalysis with dicobalt octacarbonyl effects hydrocyanation of simple terminal alkenes, styrene, conjugated dienes, and norbornenes. Unlike the nickel-catalyzed process (see below), the major products correspond to an overall Markovnikov addition of HCN (Eq. 2). Unfortunately, for many of these reactions, a relatively high reaction temperature (130°) is needed and a relatively low catalyst turnover is obtained (1–8 mol nitrile per mol Co). The use of other Co, Fe, Ni, and Pd complexes also appears in the patent literature.[2,3] Very little mechanistic information is available on most of these reactions. In sharp contrast, the mechanism of the Ni$\mathbf{L}_n$-catalyzed reaction [$\mathbf{L}$ = $(ArO)_3P$, $n = 3, 4$] is one of the most extensively studied, in part due to the commercial importance of the DuPont adiponitrile process. A comprehensive review[16] and full details of a mechanistic study[39] have been published and should be consulted for details. An abbreviated mechanism for the hydrocyanation of ethylene is shown in Scheme 1.

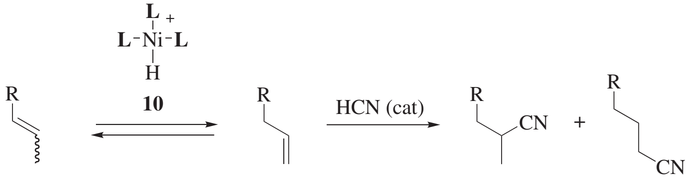
The typical hydrocyanation catalysts are zero-valent triarylphosphite-nickel complexes, $Ni[P(OAr)_3]_n$ ($n = 3, 4$; Ar = Ph or 2-, 3-, or 4-tolyl). These catalysts tolerate a broad range of substrates and functional groups. The initial step is the dissociation of the arylphosphite ligands from the Ni$\mathbf{L}_4$ complex **1** to give a coordinatively unsaturated Ni-complex that readily forms an alkene intermediate **2** (Scheme 1). Oxidative addition of HCN to this complex gives **3**. This intermediate can also be arrived at by oxidative addition of HCN to **7** and subsequent substitution of a ligand in **8** by the alkene. Loss of a ligand from **3** gives **4**. Insertion of ethylene into the metal–hydrogen bond gives **5** with a σ-bonded ethyl group and a π-bonded ethylene. With an excess of the ligand, complex **6** is produced which proceeds to give the product EtCN along with the active catalyst. The last step is essentially irreversible unless the product is an allyl cyanide. If the starting alkene is electron-deficient (tetrafluoroethylene or acrylonitrile), the reductive elimination from **6** is slow and the turnover is essentially blocked. Intermediate **5** is also the source of a deleterious side reaction which forms catalytically inactive $Ni(CN)_2$ if excess HCN is present in the medium. Several of



Scheme 1. Mechanism of the Ni-catalyzed hydrocyanation of ethylene.

the intermediates in the catalytic cycle have been identified by low-temperature spectroscopic techniques.[16]

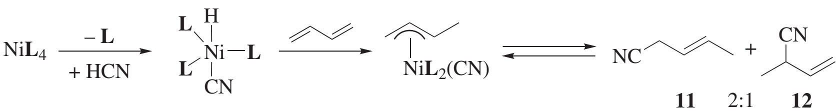
Regioselectivity. Lewis acids such as $AlCl_3$, $ZnCl_2$, or BPh_3 facilitate the addition reactions of terminal alkenes, which are otherwise slow.[21,40] In these reactions, overall anti-Markovnikov additions are observed. Internal alkenes hydrocyanate much slower than terminal alkenes and give a preponderance of linear products when isomerization is possible (Eq. 8).[21] Lewis acids (**A**) promote alkene isomerization by increasing the concentration of the cationic nickel hydride (**10**) via cyanide abstraction from the intermediate **9** by the Lewis acid. (see Scheme 1).



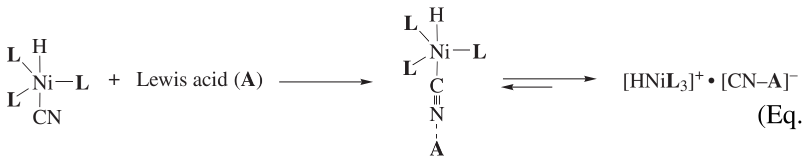
(Eq. 8)

1,3-Butadiene is readily hydrocyanated, and the resulting allylic nitriles, 3-pentenenitrile (**11**) and 2-methylbutenenitrile (**12**), are produced in a ratio of 2:1 by reductive elimination from stable and often detectable η^3-allyl nickel

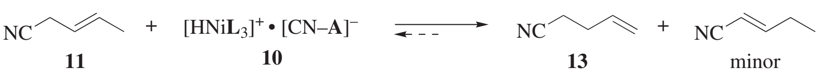
cyanides (Eq. 9). In the DuPont adiponitrile process, this reductive elimination is reversible and the nickel-catalyzed equilibration of the regioisomeric allylic nitriles is achieved at higher temperatures to favor 3-pentenenitrile (**11**). Isomerization of the 3-pentenenitrile (**11**) to the desired 4-pentenenitrile (**13**) is catalyzed by a cationic nickel hydride **10** that is generated by removal of CN^- by a Lewis acid promoter (**A** in Eq. 10). This isomerization (Eq. 11) is the result of kinetic control made possible by coordination of the CN^- to Ni.[41] Insertion of the double bond in **13** into the [Ni–H] bond of complex **10** followed by reductive elimination yields adiponitrile (**14**) (Eq. 12). It is clear that the size of the Lewis acid dictates the regioselectivity in this process, where only very little of the 2-methylglutaronitrile (**15**) is formed.



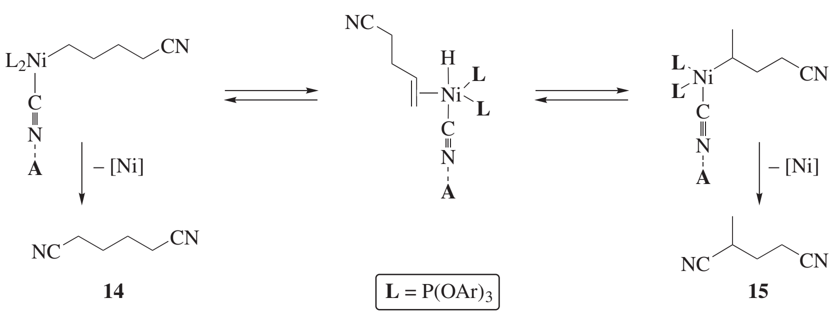
(Eq. 9)



(Eq. 10)



(Eq. 11)

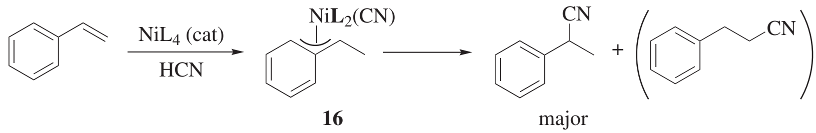


(Eq. 12)

Unconjugated dienes such as 1,5-cyclooctadiene give products typical of conjugated dienes because alkene isomerization is available through a classic insertion/β-hydride elimination mechanism.[42]

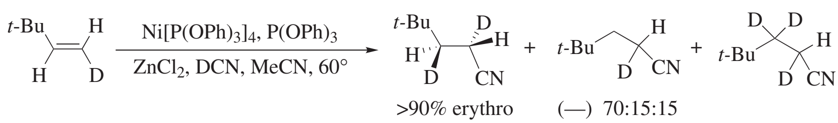
Vinylarenes, similar to conjugated dienes, give rise to η^3-benzylnickel cyanides (see Scheme 2). As a result, an overall Markovnikov addition to yield mostly the

internal nitrile ensues after the reductive elimination of Ni**L**$_2$ (Eq. 13).[16] Addition of Lewis acids to the reaction increases the proportion of the terminal nitrile.[43] The reductive elimination from the (benzyl)Ni(CN) complex **16** (or from intermediate **6** in case of simple alkenes, Scheme 1) is known to be the turnover-limiting step in the catalytic cycle.



(Eq. 13)

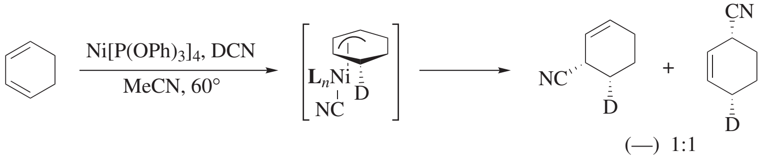
Stereoselectivity. The stereoselectivity of hydrocyanation has been studied in some detail and it has been established that the addition of HCN to olefins is stereospecifically *syn*.[23,40] Addition of HCN to 3,3-dimethyl-1-butene leads to anti-Markovnikov addition of HCN with a regioselectivity of more than 99%.[40] Addition of DCN to (*E*)-1-deuterio-3,3-dimethyl-1-butene leads predominantly to the erythro product, confirming the *syn*-addition mode (Eq. 14).[23] Significant amounts of a geminal dideuterated hydrocyanation product are also observed in this reaction, which supports the intermediacy of Ni–H intermediates. A similar reaction catalyzed by Pd(DIOP)$_2$ also leads to *syn*-addition of DCN to 4-*tert*-butylcyclohexene and *tert*-butylethylene.[44] Under these conditions norbornene gives exclusively *cis*-*exo*-bicyclo[2.2.1]heptane-3-*d*-2-nitrile.[44]



(Eq. 14)

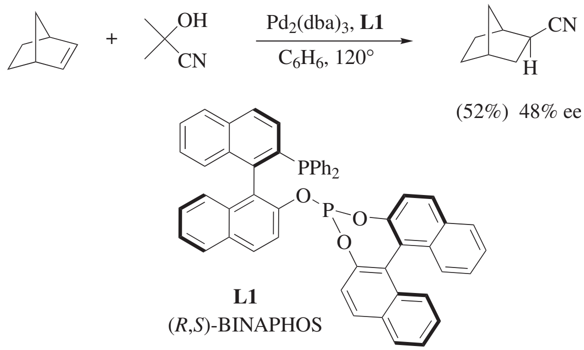
Hydrocyanation of a 1,3-diene follows a mechanism similar to that of an isolated alkene with some significant differences. In this reaction, Lewis acids are not needed and the reaction proceeds to give excellent yields.[16,42] For example, addition of DCN to 1,3-cyclohexadiene results in a smooth conversion to two monodeuterated nitriles which are 1,2 and 1,4-addition products (Eq. 15).[23] The fact that recovered cyclohexadiene does not contain any deuterium suggests that the initial metal hydride addition is irreversible in this reaction. It has been shown that the addition of HNi**L**$_3$(CN) [**L** = P(O-2-tolyl)$_3$] to butadiene is also essentially irreversible.[21] Careful analysis of the products from 1,3-cyclohexadiene suggests a *syn*-addition of DCN takes place in 1,2- and 1,4-fashions with equal propensity. Other evidence accumulated from a variety of studies including some dealing with asymmetric hydrocyanation of dienes and vinylarenes[45,46] support the intermediacy of an η^3-allyl(**L**$_n$)Ni–CN complex (Eq. 9) or an η^3-benzyl

($\mathbf{L}_n$)Ni−CN complex (Eq. 13) in the respective hydrocyanations (see below under Asymmetric Hydrocyanation of Dienes and Vinylarenes).



(Eq. 15)

Asymmetric Hydrocyanation. *Asymmetric Hydrocyanation of Norbornene.* Most of the early studies on the transition-metal-catalyzed asymmetric hydrocyanation of alkenes deal with the hydrocyanation of norbornene or its derivatives. Although high facial selectivities are observed, only modest enantioselectivities and yields are obtained in this reaction.[44,47−49] A Pd-catalyzed hydrocyanation of norbornene using the (*R*,*S*)-BINAPHOS ligand **L1** gives 48% ee for the indicated (2*S*)-product (Eq. 16).[50,51]

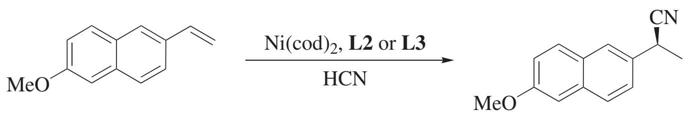


(Eq. 16)

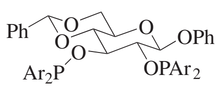
Asymmetric Hydrocyanation of Vinylarenes. The highest enantioselectivities have been obtained for the asymmetric hydrocyanation of vinylarenes using carbohydrate-based [arylphosphinite]nickel complexes as catalysts. When the 2,3-disubstituted gluco-diarylphosphinite ligand **L2** is used, for example, the naproxen precursor, 6-methoxy-2-vinylnaphthalene, is hydrocyanated with complete regioselectivity in 85−95% ee (*S*) (Eq. 17).[45,26] This catalyst system is remarkably active, giving maximum reaction rates of 2000 turnovers h^{-1} (turnover = moles of alkene/mole of Ni/unit time) and 700−800 total turnovers at room temperature.

A key finding of this work is the importance of ligand electronic effects in asymmetric catalysis. A study of the effect of the aryl substituents on phosphorus shows a pronounced increase in the enantioselectivity as the electron-withdrawing power of the substituent increases. For example, the ee in the hydrocyanation of 6-methoxy-2-vinylnaphthalene increases from 16% to 78% as the *meta*-substituents in **L2** are varied in the series Me, H, F, CF_3 (σ_m = −0.07, 0, 0.34, and 0.43,

respectively). On the other hand, ligand electronic asymmetry appears to be important in the fructose-based phosphinite ligand system **L3**. In this system, the electronic differentiation of the two phosphorus sites is used to maximize the enantioselectivity. Thus, the incorporation of a more electron-withdrawing aryl group in the C_4 position rather than in the C_3 position is crucial to obtaining the highest ee's. For example, for ligand **L3** (Eq. 17) the following selectivities are observed in the hydrocyanation of 6-methoxy-2-vinylnaphthalene: Ar^1 = 3,5-$(CF_3)_2C_6H_3$, Ar^2 = C_6H_5, 58% ee; Ar^1 = Ar^2 = 3,5-$(CF_3)_2C_6H_3$, 56% ee; Ar^1 = Ar^2 = C_6H_5, 43% ee; Ar^1 = C_6H_5, Ar^2 = 3,5-$(CF_3)_2C_6H_3$, 89% ee. A detailed account of the origin of these remarkable ligand effects and its relation to the mechanism of the asymmetric hydrocyanation has been published,[45] and the original papers should be consulted for details. Only the essential highlights are included here.



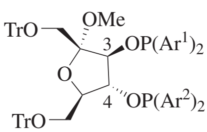
(95%) up to 95% ee



L2

	Ar
L2a	3,5-$(CF_3)_2C_6H_3$
L2b	3,5-$F_2C_6H_3$
L2c	C_6H_5
L2d	3,5-$Me_2C_6H_3$

(Eq. 17)



L3

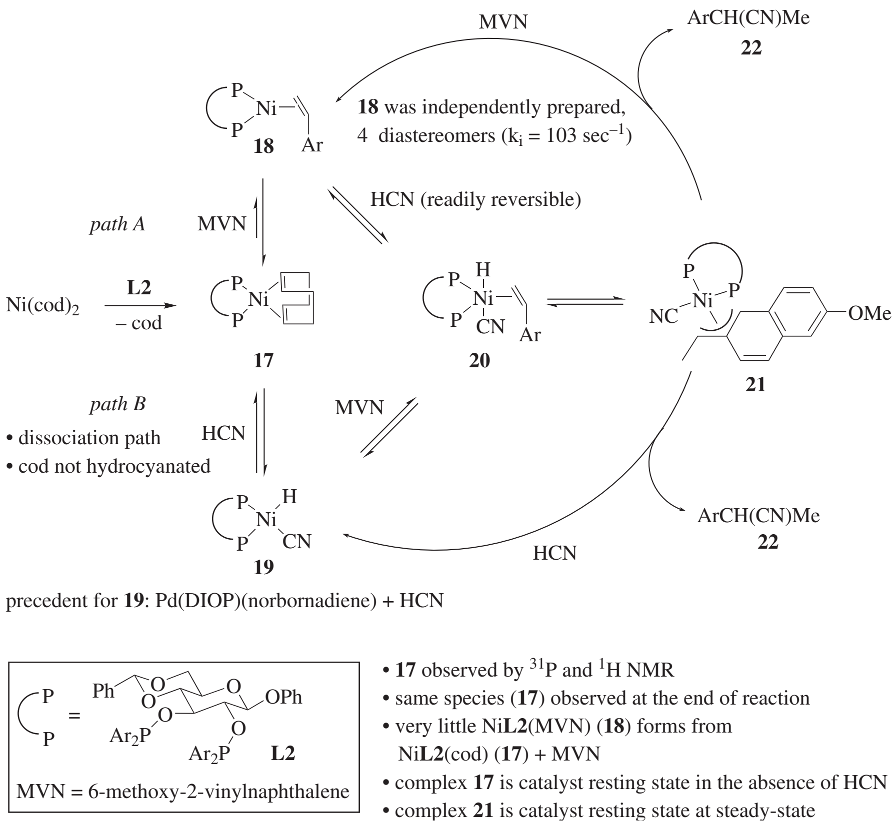
	Ar^1	Ar^2
L3a	3,5-$(CF_3)_2C_6H_3$	3,5-$(CF_3)_2C_6H_3$
L3b	Ph	Ph
L3c	3,5-$(CF_3)_2C_6H_3$	Ph
L3d	Ph	3,5-$(CF_3)_2C_6H_3$

Studies of the reaction mechanism (Scheme 2) using a series of ligands **L2** with electronically different substituents on the aromatic groups on phosphorus implicate a Ni**L2**(cod) catalyst composition **17** as the resting state in the absence of HCN.[45] However, the enantioselectivity *does not* depend on the differentiation of the *re* and *si* faces of the vinylarene in Ni**L2**(vinylarene) complex **18** that is formed from **17** by ligand exchange. Deuterium labeling studies suggest that the rate of reductive elimination from a Ni**L2**(benzyl)CN complex **21** to give product **22** increases relative to β-hydride elimination (**21** → **20**) as the electron-withdrawing power of the aryl substituent on phosphorus increases.

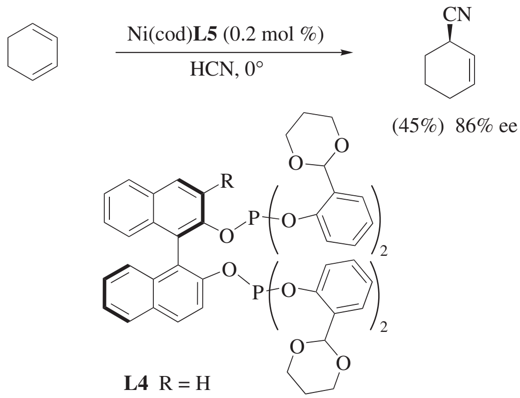
The origin of the relationship between higher enantioselectivities and electron-withdrawing aryl substituents remains speculative because the rates of many of the fundamental processes are largely unknown. Although the steric effects

are determinants of the sense of stereoinduction, the data clearly show that an electronic component is also present in this Ni**L**$_n$-catalyst system that can be used to enhance the inherent preference for the (*S*)-nitriles. A series of kinetic and isotopic labeling studies suggests that the barrier for alkene insertion and/or reductive elimination (Scheme 2) is disproportionately lower for the *S*-pathway as the electron-density at nickel is reduced, and this is the origin of the enhanced selectivity.[45]

Asymmetric Hydrocyanation of 1,3-Dienes. Addition of HCN to 1,3-cyclohexadiene in the presence of a chiral phosphite ligand **L5**, shown in Eq. 18, gives (*R*)-2-cyclohexenenitrile in 86% ee and 45% yield.[52] The 3′-methyl group in **L5** is critical for a highly enantioselective reaction since in its absence (e.g., using ligand **L4**) the selectivity is only 43% ee. Mechanistic studies in this system using DCN confirmed the earlier conclusion[45] that the enantioselectivity-determining step involves the reductive elimination from the σ-Ni(**L**)CN-allyl complex.



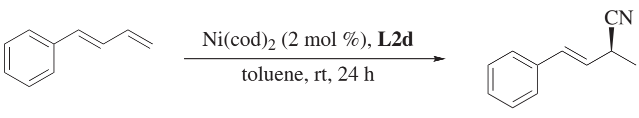
Scheme 2. Details of the mechanism of the Ni-catalyzed hydrocyanation of a vinylarene.



L4 R = H
L5 R = Me

(Eq. 18)

Carbohydrate-derived vicinal bis-diarylphosphinites (**L2**) previously used for asymmetric hydrocyanation of vinylarenes (Eq. 17) give moderate selectivities in Ni(0)-catalyzed asymmetric hydrocyanation of 1-phenyl-1,3-butadiene (Eq. 19) and other 1,3-dienes.[53]

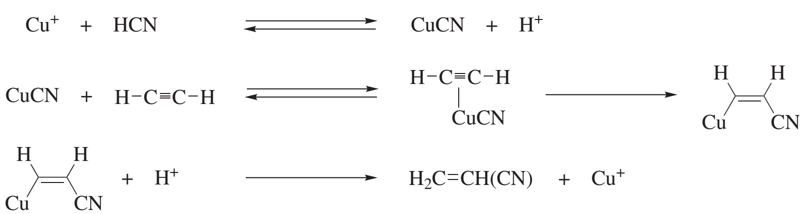


(87%) 78% ee

(Eq. 19)

Hydrocyanation of Alkynes

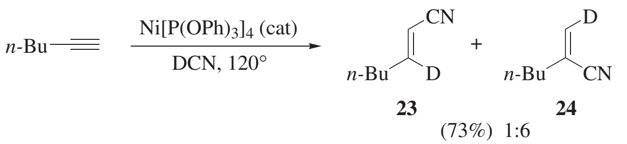
Copper(I)-Catalyzed Hydrocyanation of Acetylene. In this reaction, a dilute mixture of acetylene and hydrogen cyanide is fed into a solution of copper(I) and ammonium chloride at 70–90°. A possible mechanism for this reaction is shown in Scheme 3.[28]



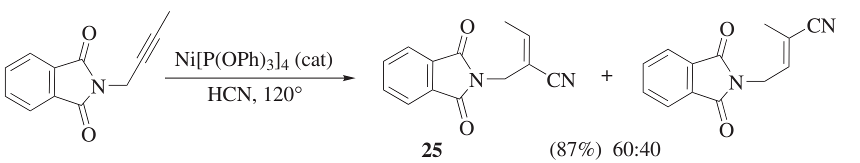
Scheme 3. Mechanism of Cu(I)-catalyzed hydrocyanation of acetylene.

Nickel(0)-Catalyzed Reactions. The mechanism of the Ni(0)(arylphosphite)-catalyzed hydrocyanation of acetylene is thought to be similar to that of alkene hydrocyanation, including the *syn*-stereoselectivity (Eq. 20).[54,55] The

regioselectivity of the reaction is largely determined by steric effects, especially when bulky substituents are present. Terminal alkynes with small and moderately sized aliphatic substituents give mostly the internal nitrile (Eq. 20, **23**:**24** = 1:6), reflecting the increased stability of the secondary C_σ−Ni bonding compared to the C−Ni bond with the terminal carbon. *tert*-Butyl and phenyl acetylenes give terminal nitriles. In hydrocyanations of alkynes containing heteroatoms on one of the substituents, there is a slight preference for the nitriles in which the nitrile group is attached to the carbon carrying the heteroatom (e.g., product **25**, Eq. 21). Hydrocyanation of internal alkynes favors the product in which the nitrile group is attached to the least hindered position. Electronic effects can play an important role in reactions of substrates with small electron-withdrawing substituents. For example, dimethyl acetylenedicarboxylate gives predominantly the *anti*-adduct, albeit in a low yield. [29]

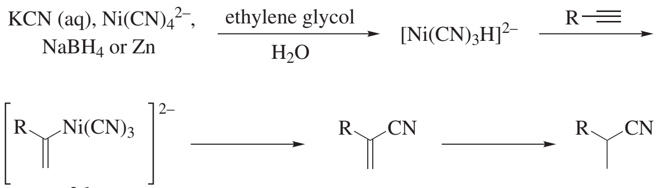


(Eq. 20)



(Eq. 21)

Potassium Tetracyanonickelate(II)-Catalyzed Reactions. The hydrocyanation/hydrogenation conditions using $K_2Ni(CN)_4$ as a catalyst (Eq. 22), which is applicable to both terminal and internal alkynes (but not to alkenes), is surprisingly ineffective for symmetrical alkynes.[31] Internal nitriles are strongly favored by this catalyst system, but unlike the nickel phosphite-catalyzed process, the regioselectivity is insensitive to substituent steric effects. Deuterium labeling studies show that borohydride is the hydrogen source for the hydrocyanation, whereas the solvent provides the hydrogens for the subsequent alkene hydrogenation. A mechanism consistent with the observed results including kinetic studies, the selective formation of the internal nitrile, and the *cis* configuration of the intermediate unsaturated nitrile involves the initial hydride transfer from a nickel−hydride species to the acetylene *without* initial formation of a π-acetylene−cyanonickelate intermediate. Subsequent cyanation of this intermediate (e.g., **26**) followed by hydrogenation gives the expected product. Formation of a $[Ni(CN)_3H]^{2-}$-complex from $[Ni(CN)_4]^{2-}$ and the solvent or sodium borohydride is assumed.[31] Presumably, the borohydride is a better source of hydrogen (as a hydride), which is consistent with the incorporation of deuterium upon use of sodium borodeuteride.



26

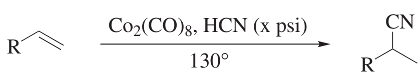
(Eq. 22)

The stoichiometric hydrocyanation of acetylenes by $CoCl_2$ and KCN under an atmosphere of hydrogen also involves formation of the related $[Co(CN)_5H]^-$ intermediate, which forms a σ-vinyl–Co intermediate.[56] The proposed mechanisms of these fascinating reactions should be considered tentative at best.

SCOPE AND LIMITATIONS

Transition-Metal-Catalyzed Hydrocyanation of Unactivated Alkenes

Addition of HCN to unactivated alkenes is a sluggish reaction that proceeds at high temperature in the gas phase over alumina,[57] cyanide-on-alumina,[57] or cobalt-on-alumina[58] catalysts. In homogeneous medium, the reaction is catalyzed by Co, Ni, and Pd complexes. For example, $Co_2(CO)_8$ facilitates the addition of HCN to alkenes in a Markovnikov fashion at 130°.[36] Propene and 1-butene give the corresponding internal nitriles in 65% and 67% conversions at 130° and with moderate pressures in an autoclave (Eq. 23). As the size of the alkyl group on the double bond increases, the conversions decrease. In the case of 1-octene, addition of triphenylphosphine improves the conversion (up to 24%). Functionalized alkenes such as methyl 5-pentenoate and 5-cyanopentene give only moderate yields under these conditions.



R	x	Time (h)	% Conv.
Me	110	15	65
Et	40	8	67
n-C_6H_{13}	46	8	5
n-C_6H_{13}	43	8	24 *Ph_3P added*

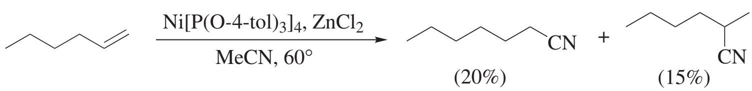
(Eq. 23)

The best results in the hydrocyanation of unactivated alkenes are obtained with $Ni[P(OAr)_3]_n$ ($n = 3$, Ar = 2-tolyl; $n = 4$, Ar = 4-tolyl), which show favorable ligand dissociation kinetics needed for the alkene activation. Olefins form complexes with $\mathbf{L}_2Ni(0)$ with equilibrium constants decreasing in the order ethylene>styrene>propene>1-hexene>disubstituted alkenes. The complexes $Ni\mathbf{L}_2$(olefin) [$\mathbf{L} = P(O\text{-}2\text{-tolyl})_3$] can be isolated for ethylene and styrene (Scheme 1).[16] Addition of HCN to this complex results in complete conversion to alkylnickel cyanide intermediates and subsequently to the products, propionitrile from

ethylene and 2-phenylpropionitrile from styrene. Other alkenes give similar intermediates, but in lower yields. Hydrocyanation of propene gives a 70:30 ratio of terminal to internal products. Isobutylene gives exclusively 3-methylbutyronitrile with cyanide addition occurring at the least hindered position. A similar regioselectivity is reported for *tert*-butylethylene.[23] Cyclopentene, cyclohexene, cyclooctene, trimethylsilylethylene, and 1,1,1-trifluropropene give the expected products in hydrocyanations using Ni[P(O-2-tolyl)$_3$]$_3$ not promoted by a Lewis acid.[16] Unfortunately, details of the preparative aspects of these reactions are sparse.

The unpromoted reactions discussed thus far generally give only a few turnovers. Since the disclosure of soluble Ni(0)[15] and Pd(0)[59] catalysts for homogeneous alkene hydrocyanation, the use of Lewis acids to promote this reaction has received a great deal of attention. The half-life of propene hydrocyanation by Ni[P(O-2-tolyl)$_3$]$_3$ is ~60 minutes at 0°.[16] The addition of Lewis acids dramatically alters the rate of the reaction, with $AlCl_3$ having the most pronounced effect: the half life at −25° is 10 minutes. Triphenylboron slows down the reaction, yet produces the best terminal to internal selectivity in the hydrocyanation of propene (89:11).

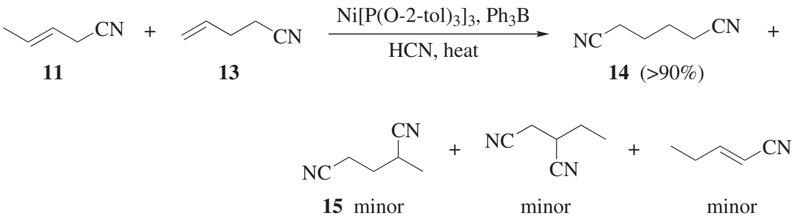
Hydrocyanation of 1-hexene catalyzed by Ni[P(O-4-tolyl)$_3$]$_4$ in the presence of excess ligand and a promoter Lewis acid such as $ZnCl_2$ gives two nitriles in terminal to internal ratio of 4:3 (Eq. 24).[40] The increased activity in the presence of added ligand is thought to be due to the prevention of the formation of the catalytically inactive **L**$_2$Ni(CN)$_2$ species. In many hydrocyanation reactions slow addition of HCN helps to slow down this deactivation process. The Lewis acid promoter acts as a cyanide acceptor and has a pronounced effect on the branched to linear ratio of products. Among the Lewis acids, $ZnCl_2$ gives one of the best selectivities in favor of the terminal nitrile of 1-hexene (terminal:internal = 78:22), whereas $AlCl_3$ is the best for internal nitrile (terminal:internal = 69:31). In the hydrocyanation of hexene with Ni[P(O-2-tolyl)$_3$]$_3$ in the presence of (4-tolyl)$_3$B, the regioselectivity for the terminal product increases to 91%. Likewise, using *p*-cresol as the solvent (Ni[P(O-4-tolyl)$_3$]$_4$:P(O-4-tolyl)$_3$:$ZnCl_2$ = 1:5:2, 60°) gives a higher proportion of the terminal product (terminal:internal = 86:14) compared with acetonitrile (terminal:internal = 78:22).[40] Isobutylene and 2,3-dimethyl-1-butene give a terminal to branched ratio of 99:1.



(Eq. 24)

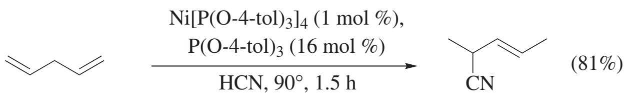
Hydrocyanation of a mixture of 3-pentenitrile (**11**) and 4-pentenenitrile (**13**) is an important step in the DuPont process for the manufacture of adiponitrile from 1,3-butadiene, and many protocols for this reaction have been described in the patent literature.[16] In this process, a mixture of mononitriles obtained from Ni(0)-catalyzed hydrocyanation of 1,3-butadiene (see below under "Hydrocyanation of 1,3-Dienes") is treated with HCN and a mixture of a Ni[P(O-2-tol)$_3$]$_3$ and Ph_3B (Eq. 25).[21,60] Because the isomerization of the internal alkene **11** to the terminal

alkene **13** catalyzed by $L_3NiH(CN)$ (Eq. 11) is faster than the hydrocyanation of the former (Eq. 12), the major product formed is adiponitrile (**14**). More robust chelating phosphites based on various biaryl scaffolds are also viable ligands,[61] including a self-assembled bidentate ligand.[61a] Many different examples have been described in the patent literature.[62]

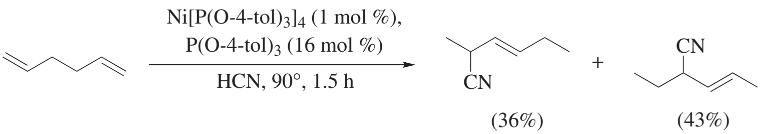


(Eq. 25)

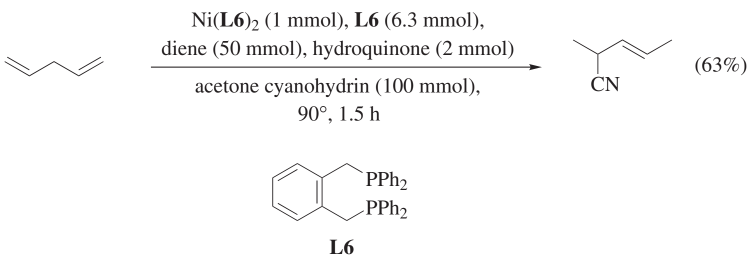
Under similar conditions non-conjugated dienes undergo hydrocyanation to give major products in which the terminal alkene is isomerized (Eqs. 26 and 27).[42] The reaction shown in Eq. 28 demonstrates the use of acetone cyanohydrin in place of toxic HCN and the use of a different chelating diphosphine (**L6**).[63]



(Eq. 26)

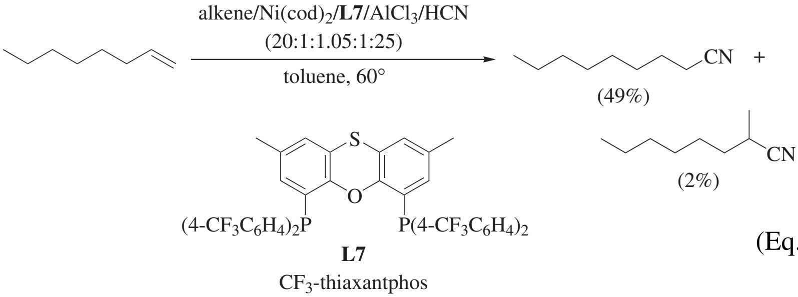


(Eq. 27)



(Eq. 28)

Rigid bidentate phosphines with an optimum bite angle of more than 100° show pronounced activity for the hydrocyanation of unactivated alkenes in the presence of Lewis acids.[64,65] Thus, $Ni(cod)_2$ in the presence of a diphosphine **L7** and $AlCl_3$ effects the hydrocyanation of 1-octene with up to 49:1 terminal to internal ratio of the isomeric nitriles (Eq. 29).[65]



(Eq. 29)

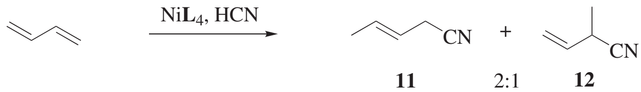
Alkenes bearing halogen, oxygen, carbonyl substituents, or other electron-withdrawing groups do not react with HCN under Ni(0)-catalysis. Mechanistic studies indicate that the final reductive elimination step is retarded by these substituents.[16]

Transition-Metal-Catalyzed Hydrocyanation of Activated Alkenes

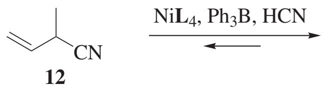
Hydrocyanation of 1,3-Dienes. Even though copper[66,67] and cobalt[3] salts and complexes have been used for the hydrocyanation of 1,3-dienes, nickel-catalyzed reactions are unparalleled in their efficiency and selectivity, and most of the known examples deal with homogeneous catalyzed reactions involving this metal. Because of the huge commercial interest in this reaction, much of the work appears in the patent literature. Only the most relevant results where full details of the preparative aspects are available are discussed here.

The DuPont process for the production of adiponitrile via hydrocyanation of butadiene represents one of the most successful commercial applications of this reaction. As shown in the accompanying equations, a triarylphosphite nickel complex catalyzes the hydrocyanation of butadiene in a multi-step process to give overall anti-Markovnikov addition of two molecules of HCN. The reaction is carried out in two stages. In the initial hydrocyanation, butadiene gives mostly a ~2:1 mixture of isomeric C_5 nitriles, 3-pentenenitrile (**11**) and 2-methyl-3-butenenitrile (**12**), which are resistant to further reaction with HCN in the absence of a Lewis acid (Eq. 30). In a second stage, the initial product is isomerized to a mixture of 3-and 4-pentenenitriles (**11** and **13**) using a $Ni[P(OAr)_3]_n$ ($n = 3$ or 4) complex and a Lewis acid such as Ph_3B or $ZnCl_2$ (Eqs. 31 and 32). Concurrent isomerization of **11** to **13** and anti-Markovnikov HCN addition to **13** follows (Eqs. 32 and 33). Under the optimum conditions, the hydrocyanation of **13** proceeds faster than all the other reactions, and adiponitrile (**14**) is formed in very high yield and selectivity (Scheme 4). The added Lewis acid promoter increases the rate of hydrocyanation of **13** and controls the selectivities in the isomerization reactions.[21,60] Major side products, 2-methylglutaronitrile (**15**) and ethylsuccinonitrile (**27**), arise from hydrocyanation of various intermediates. 2-Pentenenitrile (**28**), which is one of the isomerization products of 3-pentenenitrile, acts as an inhibitor in the process. Fortunately, only a very small amount of this

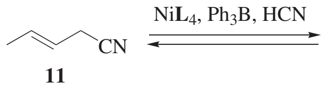
nitrile is formed under production conditions.



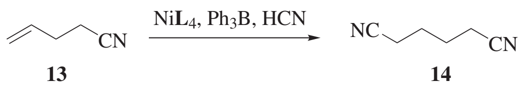
(Eq. 30)



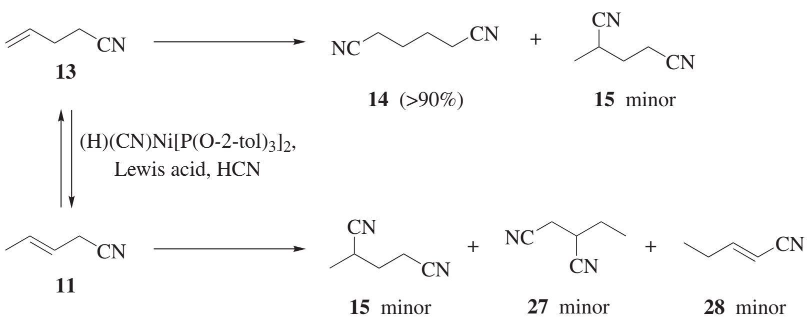
(Eq. 31)



(Eq. 32)



(Eq. 33)



Scheme 4. Side-reactions accompanying butadiene hydrocyanation.

A chelating phosphite ligand based on 2,2′-biphenol makes a robust Ni(**L8**)$_2$ complex (Fig. 1) which, remarkably, is stable when exposed to air for 14 days even in a toluene solution.[61,61a] This complex is more efficient in the initial hydrocyanation of butadiene compared with the more sensitive Ni[P(O-4-tolyl)$_3$]$_4$, yielding more than four times the turnover of the latter. Similar chelating phosphites have been described in the patent literature.[62] Two other recently developed ligands are shown in Fig. 1. The Ni-complexes of the phosphonite ligand **L9** show excellent activity and high selectivity in the hydrocyanation of butadiene.[68,68a] The triptycene-based ligand **L10** with a large bite-angle is exceptionally good in giving a high yield and a very high ratio (93:2) of 3-pentenenitrile (**11**) to 2-methyl-3-butenenitrile (**12**), especially when the reaction is carried out in dioxane (Eq. 34).[27] As might be inferred, Ni(0)-complexes of ligand **L9** and

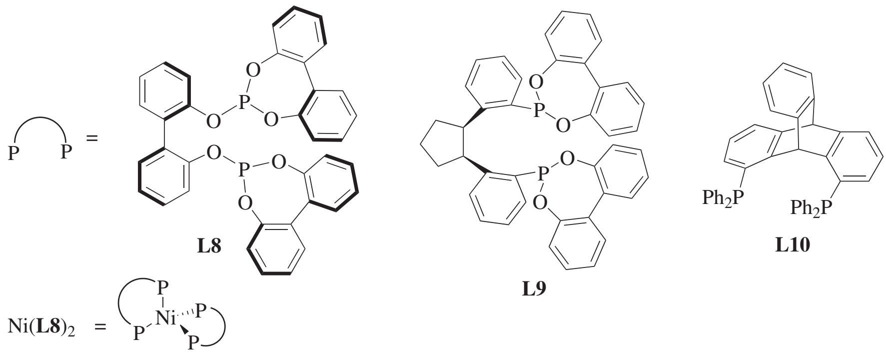
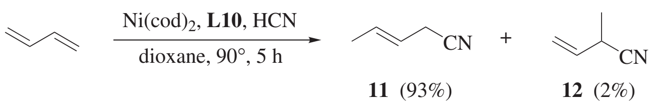


Figure 1. New ligands for hydrocyanation of 1,3-butadiene.

L10 are also good catalysts for the conversion of 2-methyl-3-butenenitrile to 3-pentenenitrile even in the absence of Lewis acids. How much this contributes to the overall higher selectivity for the formation of 3-pentenenitrile remains to be established.

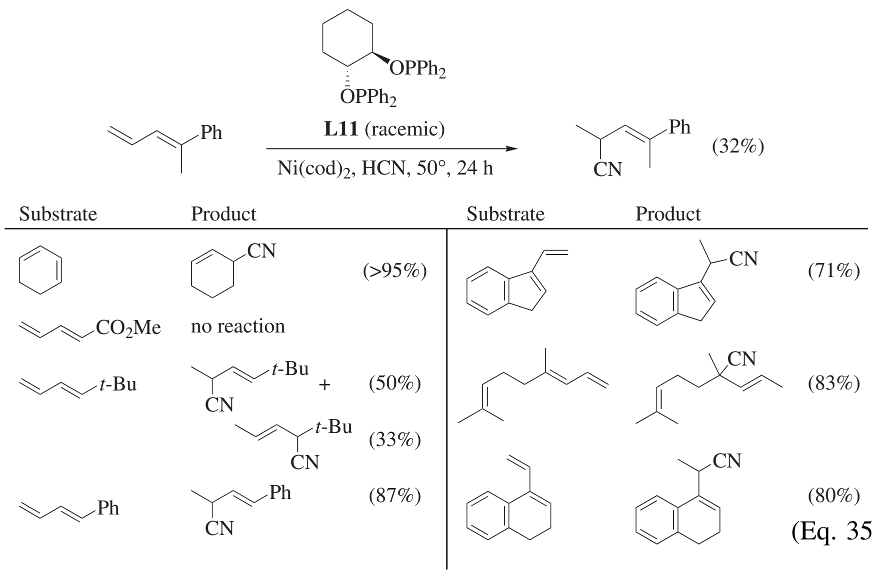


(Eq. 34)

The feasibility of hydrocyanation of other dienes catalyzed by $Ni[P(OAr)_3]_n$ ($n = 3$ or 4) has been demonstrated. These include reactions of 1-vinyl-1-cyclohexene,[16] norbornadiene,[16] dicyclopentadiene,[16] allene,[16] 1,5-cyclooctadiene,[16] 1,3-cyclooctadiene,[16] cyclopentadiene,[16] 1,3-cyclohexadiene,[23] 1-methyl-1,3-butadiene, 2-methyl-1,3-butadiene, and 1,4-dimethyl-1,3-butadiene.[42] To be of practical synthetic value, further optimization of reaction conditions will be required for most of these substrates.

A simple analog of carbohydrate-derived 1,2-bis(diarylphosphinites) (**L2**, Eq. 17), **L11**, has been used extensively in asymmetric hydrogenation and hydrocyanation reactions (see below under "Asymmetric Hydrocyanation of Vinylarenes"). The 1,2-bis(diphenylphosphinite) derived from *trans*-1,2-cyclohexanediol (**L11**) readily forms Ni-complexes that catalyze addition of HCN to a variety of 1,3-dienes at 25–50°.[53] The examples shown in Eq. 35 are typical.

Thus, sequential additions of 1,3-cyclohexadiene and HCN to a catalyst prepared from the ligand and $Ni(cod)_2$ give the expected product in >95% yield. The yields of other dienes vary with the structure of the dienes. Higher temperatures are needed for more substituted, less reactive dienes such as 1-phenyl-1-methyl-1,3-butadiene and 2,6-dimethylnona-2,6,8-triene. Depending on the structure of the diene, both 1,2- and 1,4-additions are observed.



(Eq. 35)

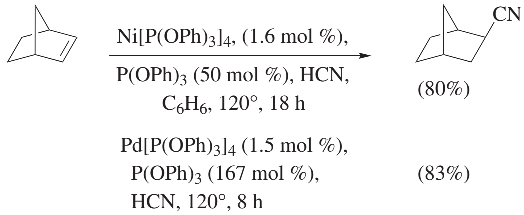
Hydrocyanation of Vinylarenes. Hydrocyanations of styrene and various other vinylarenes have been investigated in detail.[16,26,43] The internal nitrile **29** is obtained as the major product with Ni[P(O-4-tolyl)$_3$]$_4$ (Eq. 36). This can be explained on the basis of the formation of a stable η^3-intermediate (see Scheme 2, **21**)[45] whose presence can be inferred from UV spectroscopy.[16] High activity and selectivity for the formation of the internal isomer **29** has been observed using finely tuned Xantphos ligands (e.g., **L7**, see Eq. 29 for ligand structure) having a natural bite angle of 105–106°.[65] Several other catalysts that give very high regio- and enantioselectivities are discussed under "Asymmetric Hydrocyanation Reactions."

29 **30**

	Ar	**29** + **30**	**29**:**30**
Ni[P(O-4-tol)$_3$]$_4$ (5 mol %), P(O-4-tol)$_3$ (10 mol %), HCN (excess), $ZnCl_2$ (2 mol %), 88°, 3 h	4-i-BuC$_6$H$_4$	(68%)	90:10
Ni[P(O-4-tol)$_3$]$_4$ (5 mol %), P(O-4-tol)$_3$ (10 mol %), HCN (excess), $ZnCl_2$ (2 mol %), 88°, 5.5 h	6-OMe-2-naphthyl	(93%)	95:5
Ni(cod)**L7**/**L7**/styrene/HCN (1:1.05:20:25), toluene, 60°, 16 h	Ph	(90%)	99:1

(Eq. 36)

Hydrocyanation of Strained Alkenes. Hydrocyanation of norbornene is catalyzed by both Pd[P(OPh)$_3$]$_4$[59] and Ni[P(OPh)$_3$]$_4$[47,59] to give the *exo*-adduct exclusively (Eq. 37).

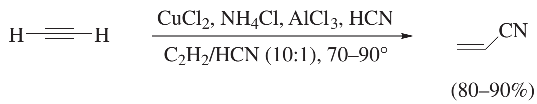


(Eq. 37)

Conjugate Addition of HCN to Activated Alkenes. As discussed in the introduction, this topic is beyond the scope of the current chapter. An excellent review of recent work has been published,[8] and the reader is directed to this source. Other pertinent references can be found in recent papers that deal with asymmetric C–CN bond-forming reactions.[13,14,69,70]

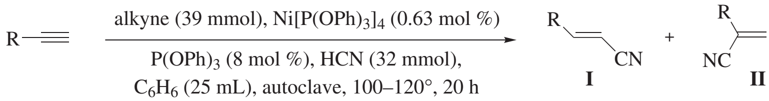
Transition-Metal-Catalyzed Hydrocyanation of Alkynes

A major manufacturing process for acrylonitrile used to be the addition of HCN to acetylene (Eq. 38) until it was replaced by the cooxidation of propylene and ammonia (the SOHIO process).[28] The need for strong acids such as HCl for catalytic activity suggests the intermediacy of a C_σ–Cu species. As expected, the major byproducts in the reaction are acetaldehyde and vinylacetylene.



(Eq. 38)

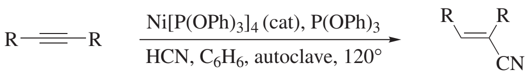
Addition of HCN catalyzed by $Ni[P(OAr)_3]_4$ to straight-chain terminal alkynes with moderately sized substituents leads to mostly the internal products (Eq. 39).[71,72] In this example, the relative stability of the secondary Ni–C_σ bond overwhelms the steric effect of the alkyl group. Symmetric alkynes give varying yields of the product (Eq. 40). Bulky substituents direct the cyano group to the terminal position, indicating that there is also a pronounced steric effect on the regioselectivity of this reaction. A similar trend is observed in silyl-substituted alkynes with 1-triphenylsilyl-1-hexyne giving exclusively the terminal nitrile (Eq. 41).[73] Trimethylsilylacetylene gives a terminal to internal ratio of 25:75 and *tert*-butyldimethylsilylacetylene gives a ratio of 35:65. The size of the silyl group can be used to control the regioselectivity in hydrocyanation reactions of disubstituted acetylenes (Eq. 41).[74] In general, the reactions proceed with *syn*-stereoselectivity. In many of these reactions, acetone cyanohydrin can be used in place of the toxic HCN, thus making this a preparatively useful reaction for the synthesis of vinyl nitrile intermediates.[72,74]



R	I + II	I:II
n-Pr	(78%)	12:88
n-Bu	(73%)	14:86
t-Bu	(15%)	88:12
t-Bu	(45%)	80:20[a]
n-C_6H_{13}	(60%)	14:86
Ph	(45%)	90:10

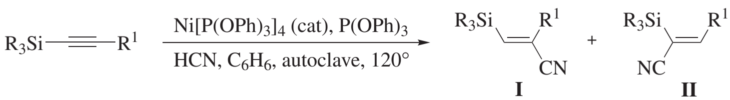
[a] Slow addition, 60°

(Eq. 39)



(Eq. 40)

R = Ph (93%)
R = CO_2Me (27%) *possibly* E-*isomer*



Me_3Si–

R^1	I + II	I:II
H	(74%)	25:75
Me	(87%)	80:20
n-Bu	(90%)	72:28
Ph	(80%)	20:80

acetone cyanohydrin, refluxing toluene

***t*-$BuMe_2Si$–**

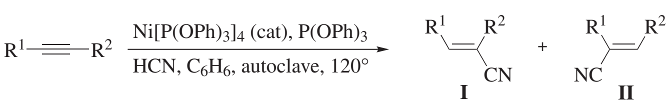
R^1	I + II	I:II
H	(57%)	35:65
Me	(88%)	98:2
n-Bu	(85%)	97:3
Ph	(73%)	90:10

Ph_3Si–

R^1	I + II	I:II
n-Bu	(75%)	100:0

(Eq. 41)

Hydrocyanations of alkynes with functionalized substituents such as hydroxy,[75] alkoxy,[76] and phthalimido (PhT)[77] have been carried out (Eq. 42). The coordinating properties of these groups can alter the commonly observed regioselectivity in some of these reactions. The products from α- and β-hydroxyalkylalkynes have been converted into α-alkylidene-γ-lactones[76] and the phthalimido-bearing nitriles[77] have been used for the synthesis of various β- and γ-amino acids via hydrogenation of the double bond followed by hydrolysis of the nitrile.[78,79]

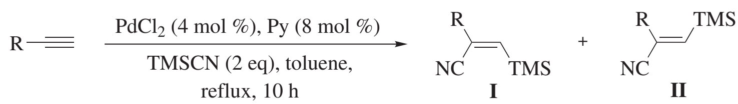


R^1	R^2	I + II	I:II
Me	CH_2OH	(72%)	1:1
H	$(CH_2)_2OBn$	(78%)	19:3
H	CH_2PhT	(88%)	4:1
H	CH_2PhT	(72%)	1:1
Me	$(CH_2)_2PhT$	(88%)	9:1

(Eq. 42)

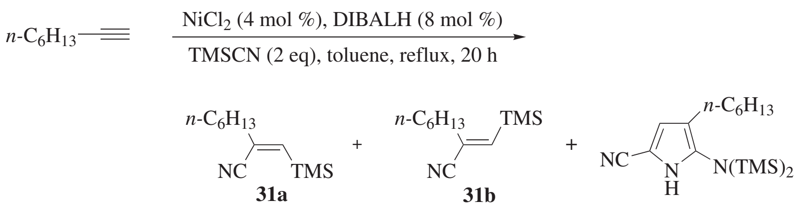
Addition of Trimethylsilyl Cyanide to Alkynes

Addition of trimethylsilyl cyanide to terminal alkynes is a synthetically useful reaction that is catalyzed by $PdCl_2$ in the presence of pyridine (Py) (Eq. 43).[80] The reaction is regioselective in that the more highly substituted nitrile is the major product, which arises via a *syn*-addition of TMSCN to the alkyne, giving predominantly the (Z)-alkene. A less general Ni(0)-catalyzed addition (Eq. 44)[80] is complicated by competitive addition of TMSCN to the initial product, yielding pyrrole carbonitriles (e.g., **31c**). Reaction with internal alkynes is sluggish and in general gives a mixture of products including pyrrole derivatives.



R	I + II	I:II
$TMSO(CH_2)_2$	(34%)	88:12
n-C_6H_{13}	(41%)	85:15
Ph	(90%)	95:5
4-$MeOC_6H_4$	(90%)	95:5
2-naphthyl	(90%)	95:5

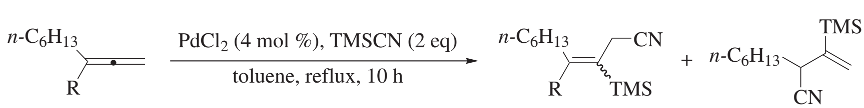
(Eq. 43)



31a + **31b** (59%) **31a**:**31b** = 72:28 **31c** (8%)

(Eq. 44)

Allenes also react with TMSCN in the presence of a $PdCl_2$/pyridine catalyst to afford vinylsilanes in which silicon is bound to the central carbon of the allene.[81] When R = H, a side product (3–20%) in which the cyanide is trapped at the C3 position is also formed (Eq. 45).



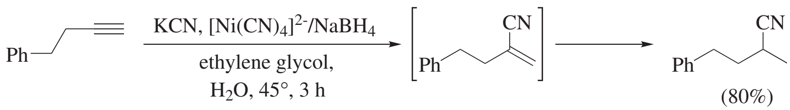
R = H (70%) E:Z = 89:11

(Eq. 45)

Cyanonickelate- and Cyanocobaltate-Catalyzed Hydrocyanation of Alkynes

An intriguing catalyst system for alkyne hydrocyanation that does not utilize organophosphorus-stabilized nickel or palladium complexes or HCN involves cyanometalates of cobalt and nickel in mixed aqueous media. On the basis of initial work involving the stoichiometric hydrocyanation of alkynes with $[Co(CN)_5H]^{3-}$,[82] a catalyst employing $Ni(CN)_4{}^{2-}$ for the hydrocyanation of alkynes has been developed.[31,56] As shown in Eq. 46, treatment of an alkyne with

KCN, a reducing agent such as Zn or $NaBH_4$, and a substoichiometric amount of $Ni(CN)_4^{2-}$ leads to alkyne hydrocyanation and subsequent hydrogenation of the initially formed unsaturated nitrile. Attractive features of this system include the use of an air- and moisture-stable catalyst precursor, the use of the cyanide ion as both a reagent and a ligand for the catalyst, and the ease of separating an aqueous catalyst solution from the product and substrate. One major drawback is the low catalyst turnover (<8 mol RCN/mol Ni).

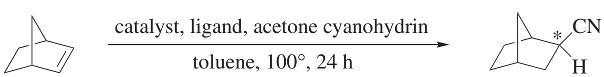


(Eq. 46)

Asymmetric Hydrocyanation Reactions

Markovnikov addition of HCN to an alkene can in principle serve as an entry into chiral compounds that can be transformed into a wide array of useful products.[26,83] In spite of the extensive work on hydrocyanation of alkenes, only limited research activity has been directed toward finding an asymmetric variation of this reaction.

Bicyclo[2.2.1]heptanes. Most of the early studies in this area focused on the HCN additions to norbornene and its derivatives (Eq. 47). Although these reactions give exclusively the *exo*-isomer, the highest enantiomeric excess reported to date for this class of substrates is only ~55%, using a binaphthol-derived phosphite **L12** (Fig. 2) as a ligand for Ni(0).[51] Other ligands that have been investigated for this reaction include **L13**,[49] **L1**,[50], DIOP,[47] and BINAP,[48] whose structures are shown in Fig. 2. The yields and enantioselectivites obtained with these ligands using either their nickel or palladium complexes are also shown (Eq. 47).



Catalyst, Ligand		% ee	Config.
$Ni(cod)_2$, **L12**	(—)	55	—
$Ni(\mathbf{L13})_2$, Ph_3B	(58%)	38	*R*
$Ni(cod)_2$, **L1**	(52%)	40	*S*
$Pd(\mathbf{L1})_2$, **L1**	(52%)	48	*S*
Ni[(*R*,*R*)-DIOP]$_2$, (*R*,*R*-DIOP)	(20%)	14	*R*
Pd[(*S*,*S*)-DIOP]$_2$, (*S*,*S*-DIOP)	(94%)	32	*S*
Pd[(*R*)-BINAP]$_2$, (*R*)-BINAP	(6%)	40	*R*

(Eq. 47)

Norbornadiene and benzonorbornene have also been hydrocyanated with low enantioselectivites using (−)-Pd(DIOP)$_2$ complexes.[47] The ligand **L12** gives an ee of 73% in the asymmetric hydrocyanation of vinyl acetate in a low-yielding reaction.[51]

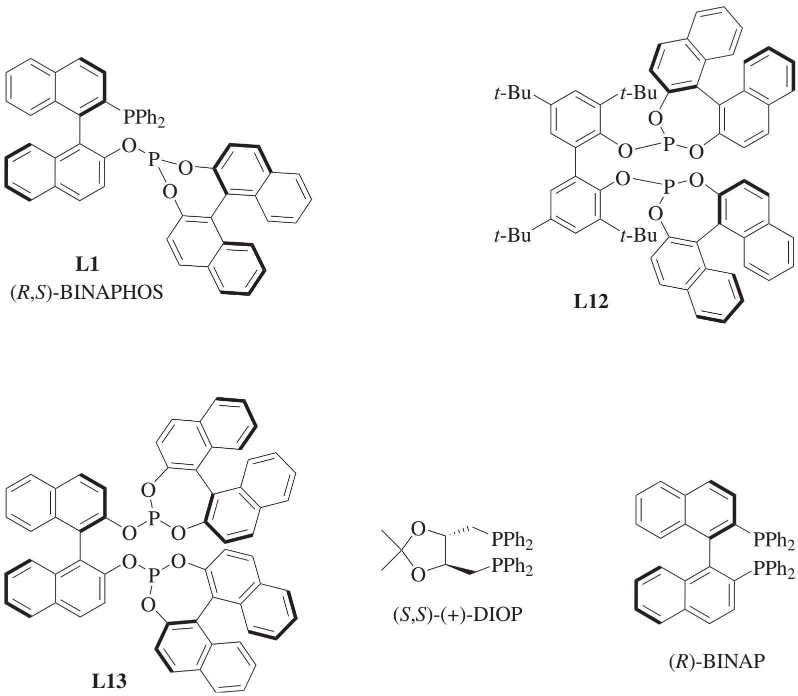
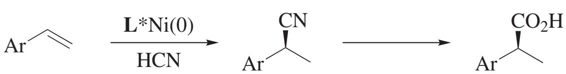


Figure 2. Ligands for asymmetric hydrocyanation of alkenes.

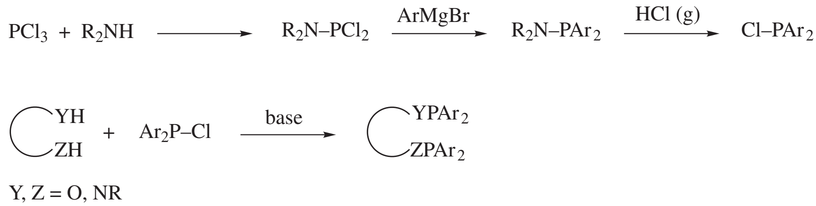
Vinylarenes. An important class of compounds that can be readily prepared from vinylarenes via the asymmetric hydrocyanation route are the 2-arylpropionitriles, precursors for the widely used antiinflammatory 2-arylpropionic acids (Eq. 48).[84,85] Of these, only naproxen [(*S*)-2-(6-methoxynaphthyl) propionic acid] is sold as an enantiomerically pure drug. Racemic ibuprofen and naproxen have been prepared by the Ni[P(O-4-tolyl)$_3$]$_4$-catalyzed hydrocyanation of the corresponding vinylarene (Eq. 36) followed by hydrolysis of the resulting 2-arylpropionitrile.



(Eq. 48)

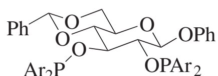
Ar = 4-isobutylphenyl (ibuprofen)
Ar = 6-methoxy-2-naphthyl (naproxen)

The most active ligands for the hydrocyanation of vinylarenes are vicinal diarylphosphinites derived from 1,2-diols. Readily accessible diarylchlorophosphines can be coupled to several commercially available diols and amino alcohols (Scheme 5). Hydrocyanations of prototypical vinylarenes using phosphinites from dimethyl tartrate, binaphthol, propranolol, pseudoephedrine, prolinol, pinenediol,



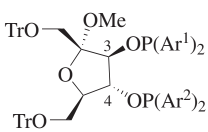
Scheme 5. Synthesis of diarylphosphinites.

and various steroidal diols as ligand precursors give excellent yields and regioselectivities, yet only disappointing enantioselectivities.[83] However, these studies established that the 1,2-bis(diarylphosphinites) could serve as broadly applicable ligands for the Ni(0)-catalyzed hydrocyanation of vinylarenes.



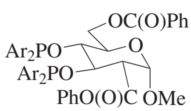
L2

	Ar
L2a	3,5-$(CF_3)_2C_6H_3$
L2b	3,5-$F_2C_6H_3$
L2c	C_6H_5
L2d	3,5-$Me_2C_6H_3$



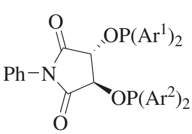
L3

	Ar^1	Ar^2
L3a	3,5-$(CF_3)_2C_6H_3$	3,5-$(CF_3)_2C_6H_3$
L3b	Ph	Ph
L3c	3,5-$(CF_3)_2C_6H_3$	Ph
L3d	Ph	3,5-$(CF_3)_2C_6H_3$



L14

	Ar
L14a	3,5-$(CF_3)_2C_6H_3$
L14b	Ph
L14c	3,5-$Me_2C_6H_3$



L15

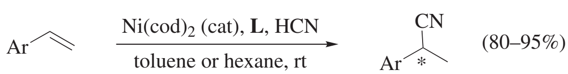
	Ar^1	Ar^2
L15a	3,5-$(CF_3)_2C_6H_3$	3,5-$(CF_3)_2C_6H_3$
L15b	Ph	Ph
L15c	Ph	3,5-$(CF_3)_2C_6H_3$

Figure 3. Carbohydrate-derived ligands for asymmetric hydrocyanation of vinylarenes.

The highest enantioselectivities for the asymmetric hydrocyanation of vinylarenes have been obtained using finely tuned carbohydrate-derived phosphinite–Ni catalysts. Several 1,2- and 1,3-diarylphosphinite ligands are synthesized from tartaric acid and from various sugars including glucose, galactose, fructose,

2-acetamidoglucose, lactose, and trehalose.[83] The structures of four of these scaffolds **L2**, **L3**, **L14**, and **L15**, along with the substituents on the *P*-aryl groups, are shown in Fig. 3.

The results of hydrocyanation of vinylarenes using these ligands are shown in Eq. 49 and the tables that follow.[83] Inspection of the results in Table A suggests that the local chirality defined by the phosphinoxy-bearing carbons controls the absolute configuration of the major product. Thus, ligands of the type 2,3-*O*-disubstituted D-gluco-bis(diarylphosphinite) (**L2**) give the (*S*)-nitrile as the major product, whereas the corresponding 3,4-bis-*O*-diarylphosphinites (**L14**) give the (*R*)-nitrile. In a related observation, 3,4-disubstituted methyl α-D-fructofuranoside 3,4-*O*-bis(diarylphosphinites) (**L3**) also give the (*R*)-nitrile. These and other initial results suggest that the phenyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**L2**) is the best and most accessible sugar backbone, and further variations of the *P*-aryl-substituent on this sugar backbone have been undertaken to enhance the observed enantioselectivity. As shown in Table B, two strongly electron-withdrawing CF_3-substituents at the 3- and 5-positions of the arylphosphinites (ligand **L2a**) give the highest selectivity in the asymmetric hydrocyanation of a number of vinylarenes. The ee's decrease dramatically (from >85% to 16% for 6-methoxy-2-vinylnaphthalene) as the electron-withdrawing power of the *P*-aryl substituent decreases (for **L2a**–**L2d**, $\sigma_m = 0.43, 0.34, 0, -0.07$ respectively).



(Eq. 49)

The asymmetric hydrocyanations of a series of 4-substituted styrenes show that the electron-deficient catalysts indeed give the highest ee's in every case examined (e.g., for 4-methylstyrene: **L2a**, 70%; **L2b**, 47%; **L2c**, 1%).[45] Yet the electronic nature of the substrate also seems to play an important role. For example, the following ee's are observed using **L2a** for a series of substituted styrenes: 4-Me, 70%; 4-Ph, 68%; 4-phenoxy, 60%; 4-*i*-Bu, 56%; 4-MeO, 52%; 4-Cl, 40%; 4-F, 28%; 4-CF_3, 14%.

Fine-tuning of the diaryl phosphinites derived from the methyl α-fructofuranoside (**L3**) produces electronically 'symmetrical' and 'unsymmetrical' bis(diaryl) phosphinite ligands that afford (*R*)-2-arylpropionitriles (Table C).[86] As anticipated from previous work, electron-donating substituents on the phosphorus aryl groups give the lowest enantioselectivities. Symmetrical electron-deficient

TABLE A. EFFECT OF SUGAR BACKBONE ON CONFIGURATION OF THE HYDROCYANATION PRODUCT OF 6-METHOXY-2-VINYLNAPHTHALENE

Ligand	Ar	% ee	Config.
L2c	Ph	35	*S*
L14b	Ph	20	*R*
L3b	Ph	43	*R*

TABLE B. EFFECT OF ELECTRON-WITHDRAWING GROUPS ON ENANTIOSELECTIVITY

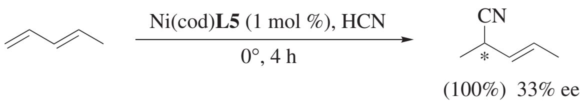
	Ligand, % ee, *S*			
Vinylarene	**L2a**	**L2b**	**L2c**	**L2d**
6-MeO-2-vinylnaphthalene	85–91	78	35	16
2-vinylnaphthalene	77	75	46	45
1-vinylnaphthalene	68	—	63	—
acenaphthene	59	—	0	—
3-fluoro-4-phenylstyrene	55	—	10	—
4-isobutylstyrene	56	38	6	—
4-trifluoromethylstyrene	14	9	1	—

TABLE C. EFFECT OF ELECTRONIC ASYMMETRY ON ENANTIOSELECTIVITY OF THE HYDROCYANATION PRODUCT OF 6-METHOXY-2-VINYLNAPHTHALENE

Ligand	% ee, *R*	Ligand	% ee, *S*
L3a	56	**L15a**	70
L3b	43	**L15b**	54
L3c	58	**L15c**	77
L3d	89		

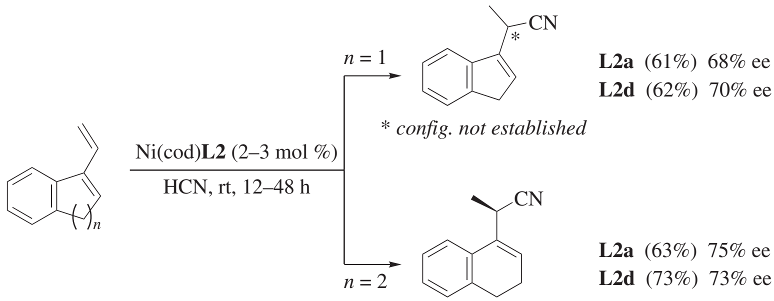
phosphinites increase the selectivity to some extent. But the highest enantioselectivities (89–95% ee) are obtained with C_3 of the sugar carrying an electron-rich phosphinite, and the C_4 carrying an electron-deficient phosphinite (ligand **L3d**). A similar observation is also made using (3*S*,4*S*)-tartranil phosphinites (**L15**): the highest ee, 77% (*S*), is obtained with a mixed phenyl/3,5-bis(trifluoromethyl)phenyl derivative (**L15c**) whereas the C_2-symmetric 3,5-bis(trifluoromethyl)phenyl- and phenylphosphinite derivatives **L15a** and **L15b** give 70 and 54% ee, respectively.

1,3-Dienes. Asymmetric hydrocyanation of 1,3-dienes continues to be a challenge. The best results reported to date are for a low-yielding reaction of 1,3-cyclohexadiene with HCN using a Ni(0)-complex of a binaphthol-derived phosphite **L5** (Eq. 18).[87] Under the same conditions, 1-methylbutadiene gives an ee of 33% (Eq. 50).

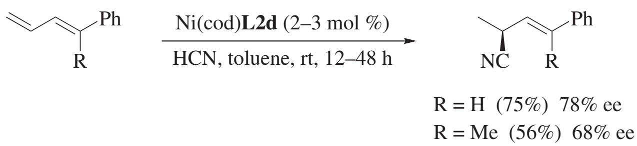


(Eq. 50)

The D-glucose-derived ligands **L2a** and **L2d** (Fig. 3) used for asymmetric hydrocyanation of vinylarenes are moderately effective for the hydrocyanation of special classes of 1,3-dienes, as shown in Eqs. 51 and 52.[53]



(Eq. 51)



(Eq. 52)

Limitations and Future Prospects

Currently, synthetically useful hydrocyanation reactions are limited to vinylarenes, certain types of 1,3-dienes, and alkynes. Reactions of unactivated terminal alkenes proceed in moderate yields and regioselectivities. Intermediacy of an allylnickel complex in the 1,3-diene hydrocyanation leads to good-to-moderate regioselectivity in reactions of substituted 1,3-dienes. Isomerization of double bonds under hydrocyanation conditions limits the utility of internal and unconjugated dienes. The regioselectivity in the hydrocyanation of internal alkynes is poor, although terminal silyl substitution and judicious use of alkynes carrying heteroatom-substituted side-chains do provide a synthetically viable route to complex vinyl nitriles. Unactivated alkenes are less reactive and need Lewis acids to promote the reaction. While the $Co_2(CO)_8$-mediated reactions give the Markovnikov products selectively from terminal alkenes, high temperatures, prolonged reaction times, and low turnovers in the catalyst are major drawbacks of this otherwise worthwhile hydrofunctionalization reaction. A systematic investigation of the cobalt-mediated reaction might be a highly profitable area for future research. Reactions of allenes have not been explored to a great extent. Asymmetric hydrocyanation is another potentially important area that has been poorly developed. Enantioselectivities above 90% ee have been achieved only for vinylnaphthalene derivatives. Substituted dienes, which undergo hydrocyanation reactions even in the absence of Lewis acids, could in principle serve as highly valuable precursors if the problems of regio- and stereoselectivities can be solved. Alkenes carrying electron-withdrawing substituents do not participate in metal-catalyzed hydrocyanation reactions. These substrates are ideally suited for the base- or Lewis acid catalyzed reactions. Finally, the toxicity of HCN is an important consideration, even though with proper precautions it can be readily

handled as borne out by the use of billions of pounds of HCN in the chemical industry. Use of acetone cyanohydrin and TMSCN as surrogates for the toxic HCN should alleviate some of the safety concerns.

APPLICATIONS TO SYNTHESIS

The synthesis of adiponitrile by the Ni(0)-catalyzed hydrocyanation of 1,3-butadiene is one of the largest industrial applications of homogeneous catalysis.[22,88] The nitrile is reduced and the resulting hexamethylenediamine is used for various applications including the manufacture of nylon-66. The antiinflammatory 2-arylpropionic acids ibuprofen and naproxen have been synthesized in racemic form by hydrocyanation of the corresponding vinylarenes.[43] An asymmetric version of this reaction would be useful for the synthesis of enantiopure (*S*)-naproxen since the precursor 2-arylpropionitrile can be recrystallized to enantiomeric purity.[89] Hydrocyanation of functionalized alkynes has been used for the syntheses of α-alkylidene-γ-lactones[76] and β- and γ-amino acids.[78,79] Conjugate addition of HCN or its surrogates including asymmetric enantioselective versions have been reported and these reactions have been used extensively in synthesis. A discussion of these reactions is beyond the scope of this chapter and other sources should be consulted for details.[8,13,14]

COMPARISON WITH OTHER METHODS

Nitriles can be prepared by replacement of halides and activated alcohol derivatives (e.g., tosylates, mesylates).[90–94] These reactions proceed better in polar aprotic solvents such as DMSO.[95–97] Phase-transfer catalysts (e.g., hexadecyltributylphosphonium bromide) permit the synthesis of octylcyanide from 1-chlorooctane.[98–100] Catalysis by crown ethers such as 18-crown-6 is also useful for the synthesis of a variety of primary and, occasionally, secondary cyanides from the corresponding halides.[101] Dehydrations of aldehyde oximes, carboxamides,[102] and reactions of carbonyl compounds with tosylmethyl isocyanide (TosMIC)[103,104] also give nitriles. Ring-opening reactions of epoxides,[105–108] aziridines,[109,110,111] and activated cyclopropanes[112,113] offer other attractive routes to highly functionalized nitriles. Vinylnitriles, the products of alkyne hydrocyanation, can be synthesized by Pd(0)-catalyzed reaction of vinyl bromides with cyanide ion in a stereospecific reaction.[114] A mild cobalt-catalyzed hydrocyanation of olefins using a combination of tosyl cyanide and phenylsilane proceeds with Markovnikov regioselectivity and is useful for the synthesis of even tertiary cyanides from 1,1-disubstituted alkenes.[115]

EXPERIMENTAL CONDITIONS

Safety in the Use of Hydrogen Cyanide

Hydrogen cyanide is a highly toxic, volatile liquid (bp 26°) that is also susceptible to explosive polymerization in the presence of base catalysts. Considering

its extensive use in industry, reports of accidents are rare, pointing to the extreme diligence and attention paid during manufacturing processes. In the laboratory it should be used only in small quantities in a well-ventilated hood. Other sensible precautions include not working alone and having available proper first aid equipment, HCN monitors, and Scott Air Packs. Large quantities of HCN should be handled by a team of at least two technically qualified individuals who have received appropriate medical training for treating HCN poisoning.[116] On an industrial scale, HCN is disposed of by burning. Smaller amounts such as are used in a typical laboratory setting can be disposed of by adding to an equimolar mixture of sodium hydroxide and sodium hypochlorite (which converts it to the cyanate).

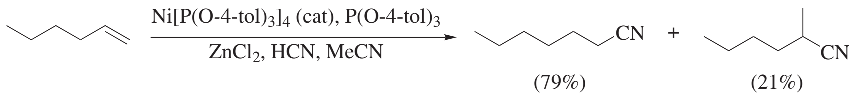
Sources of Hydrogen Cyanide

Hydrogen cyanide is commercially available from Fumico Inc. (PO Box 3459, Amarillo, TX 79106). Commercial HCN is stabilized with small amounts of strong acids such as H_2SO_4. In the laboratory HCN may be prepared by adding concentrated sulfuric acid to sodium cyanide and distilling the product formed into a cold trap, as described by Ziegler and co-workers.[117,118] Small amounts of HCN may be purified by vacuum transfer through Drierite. A standard solution of HCN may be prepared by adding the appropriate amount of pre-cooled solvent to a measured volume of HCN collected in a cold trap. Such solutions, stabilized by adding a trace of P_2O_5, can be stored in a freezer for subsequent use. Small amounts of uninhibited HCN should be stored below its mp ($-13°$). It is most conveniently transferred cold at low temperature using a pre-cooled cold syringe (density 0.687 g mL^{-1}). Acetone cyanohydrin and trimethylsilyl cyanide, often used as alternatives, are commercially available and should be treated with care, especially if formation of HCN or large concentrations of cyanide salts are possible under the reaction conditions or during work up.

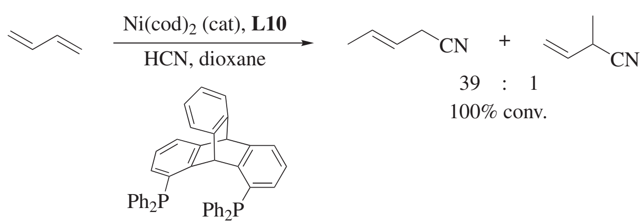
Catalysts

Because of the air sensitivity of nickel(0) complexes, small-scale reactions start with preparation of these complexes in a drybox or under strict anaerobic conditions. The most commonly used arylphosphite–Ni complexes Ni[P(O-2-tolyl)$_3$]$_3$,[119] Ni[P(O-4-tolyl)$_3$]$_4$,[120] and Ni[P(O-phenyl)$_3$]$_4$,[121] are prepared by well-known procedures. The hydrocyanation reactions may be carried out neat in the starting alkene, diene, or alkyne, or in various solvents including benzene, toluene, xylenes, acetonitrile, or dioxane. Because one of the major catalyst deactivation paths involves the reaction between Ni(0)[L]$_n$ and HCN to form $Ni(CN)_2$, it is often advantageous to add HCN slowly to a mixture of the substrate and the precatalyst in the appropriate solvent. Excess amounts of HCN are purged before isolating the product using standard organic chemistry techniques. In one of the most common protocols, especially when chelating ligands are involved, the catalyst is generated in situ by the reaction of a readily available Ni(0) source such as Ni(cod)$_2$ with the ligand. Catalytically active Ni(0) complexes can also be prepared by reduction of Ni(II) salts[122] with activated zinc in the presence of a ligand.[45]

EXPERIMENTAL PROCEDURES

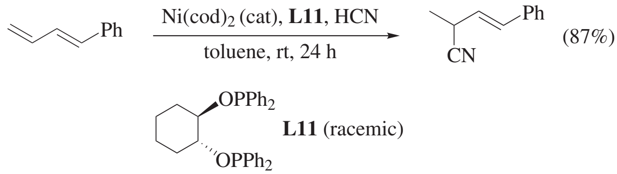


Heptanenitrile and 2-Methylhexanenitrile [Ni(0)-Catalyzed, Lewis Acid Promoted Hydrocyanation of a Terminal Alkene].[40] Tetrakis(tri-4-tolylphosphite)Ni(0) (1.4 g, 0.001 mol), $ZnCl_2$ (0.024 g, 0.002 mol) and tri-4-tolylphosphite (1.75 g, 0.005 mol) were charged to the reaction flask under heavy nitrogen purge. Hex-1-ene (25 mL, 0.2 mol) and acetonitrile (25 mL) were then added and the mixture was heated with stirring to 60°. When equilibrium temperature had been reached, HCN was continuously fed into the reaction mixture by passing a stream of dry nitrogen through a trap containing liquid HCN at 0°. After 2.5 hours, 1.90 mL (0.05 mol) of HCN had been added to the system. GC analysis on a 10-ft. column (10% SE-30 on Chromosorb W) indicated that the nitriles produced (total, 5.5 g) consisted of 79.4% heptanenitrile and 20.6% 2-methylhexanenitrile. The nitriles were identified by NMR, IR, and mass spectrometry, and their properties matched those of the commercially available materials.

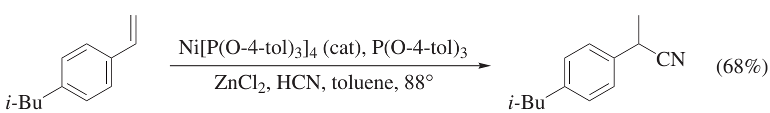


L10

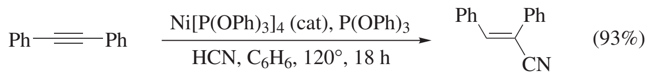
3-Pentenenitrile [Ni-Catalyzed Hydrocyanation of a 1,3-Diene].[27] A solution of ligand **L10** (11.5 mg, 0.018 mmol) in 2 mL of solvent was added to $Ni(cod)_2$ (5.0 mg, 0.018 mmol). Cooled liquid butadiene (200 μL, 2.29 mmol, 125 equiv) was added by an Eppendorf pipette, followed by 50 μL of *n*-decane as an internal standard. The solution was transferred into a 15-mL Schlenk tube equipped with a Teflon-coated stirring bar. A round-bottom Schlenk flask was filled with 1 mL of dioxane and an excess of HCN (13 μmol/min), which was taken up in a 5-mL syringe and was added to the reaction mixture by syringe pump during 3 hours (closed system). The mixture was stirred for another 5 hours at 90°. The reaction product was cooled to 0° and flushed with a gentle stream of argon for 1 minute to remove traces of HCN. Samples were analyzed by GC, using *n*-decane as internal standard. The reaction showed 100% conversion after 5 hours, with 93.3% of the product as *trans*-3-pentenenitrile and 2.4% as 2-methyl-3-butenenitrile. All the reactions were carried out in duplicate, showing a variability for conversion and selectivity of ±2% and ±1%, respectively.



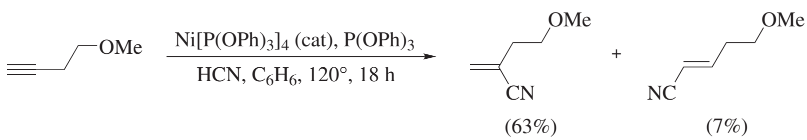
(*E*)-2-Methyl-4-phenylbut-3-enenitrile [Ni(0)-Catalyzed Hydrocyanation of an Activated Diene.][53] To a mixture of the 1,2-bisdiphenylphosphinite ligand **L11** (0.05 mmol) and $Ni(cod)_2$ (0.05 mmol) in the drybox was added 0.2 mL of toluene, and the mixture was stirred for 5 minutes at room temperature. Subsequently, 0.2 mL of a toluene solution of the diene (0.5 mmol) was added dropwise, and the reaction mixture was stirred for 10 minutes at room temperature. Then 0.2 mL of 2 M HCN in toluene was added slowly, dropwise, and the reaction mixture was stirred for 20 hours at room temperature. The reaction flask was removed from the drybox, and N_2 gas was passed into the reaction mixture in a well-ventilated hood to remove excess HCN. On larger scales, the HCN/N_2 mixture should be trapped in a solid KOH tower. The crude mixture was passed through a small pad of silica to remove the catalyst and the solvent was removed under vacuum. The product was purified by silica gel column chromatography using 100% hexane to hexane/Et_2O (19:1) as eluents to afford the pure product (87% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (d, $J = 7.5$ Hz, 3 H), 3.52 (m, 1 H), 6.07 (dd, $J = 6.5$, 15.5 Hz, 1 H), 6.75 (d, $J = 16$ Hz, 1 H), 7.3–7.42 (m, 5 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 19.06, 28.38, 120.9, 124.38, 126.57, 128.29, 128.74, 132.55, 135.74.



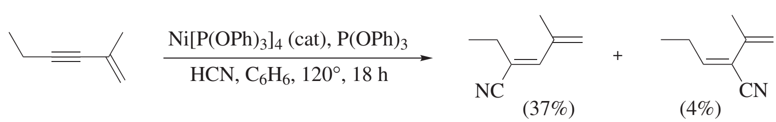
2-(4-Isobutylphenyl)propionitrile [Ni(0)-Catalyzed Hydrocyanation of a Vinylarene].[43] Tetrakis(tri-4-tolylphosphite)nickel(0) (1.50 g, 1.0 mmol) and tri-4-tolyl phosphite (0.30 mL, 1.0 mmol) were dissolved in toluene (30 mL). Zinc chloride (0.06 g, 0.5 mmol) was dissolved in propionitrile (0.5 mL) and then added to the catalyst mixture, which was subsequently heated to 88° under nitrogen. 4-Isobutylstyrene (3.45 g, 21.5 mmol) was added by syringe pump; 0.30 g was added initially and the remainder added at 1.33 mL/h. After the initial addition of the substrate, HCN/N_2 was fed at 3 mL/min for 3 hours and then at 1 mL/min for 3 hours. Silica gel chromatography of the reaction mixture (hexane/EtOAc) afforded the title product (2.66 g, 14.2 mmol, 68% yield) as a colorless liquid; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.90 (d, $J = 7$ Hz, 6 H), 1.61 (d, $J = 7$ Hz, 3 H), 1.76–1.94 (m, 1 H), 2.47 (d, $J = 7$ Hz, 2 H), 3.86 (q, $J = 7$ Hz, 1 H), 7.14 (d, $J = 8$ Hz, 2 H), 7.25 (d, $J = 8$ Hz, 2 H). Anal. Calcd for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.31; H, 8.95; H, 7.47.



(*E*)-2,3-Diphenylprop-2-enenitrile [Ni(0)-Catalyzed Hydrocyanation of a Disubstituted Alkyne].[55] Into a 75-mL stainless-steel autoclave was placed $Ni[P(OPh)_3]_4$ (0.24 g, 0.2 mmol), $P(OPh)_3$ (0.8 g, 2.5 mmol), diphenylacetylene (7 g, 39 mmol), HCN (1.25 mL, 32 mmol), and benzene (25 mL). The vessel was heated at 120° for 18 hours. After the reaction mixture was cooled, benzene was removed by distillation. Column chromatography (basic alumina, activity II, elution with 10% ether in light petroleum), followed by distillation, afforded the unsaturated nitrile (6.12 g, 93% yield) as colorless crystals; mp 48–49°; bp 130° (oven temperature)/0.01 mmHg; IR 2225 cm^{-1}; ^1H NMR (60 MHz) δ 7.33 (s, 5 H, Ar), 7.47 (s, 6 H, Ar-H); ^{13}C NMR (22.62 MHz) δ 114.43, 120.15, 128.61, 128.93, 129.13, 129.32, 129.84, 132.70, 133.61, 144.21; MS m/z: 205. No trace of polymerized or disubstituted material was detected. When the HCN was replaced by acetone cyanohydrin the yield of the nitrile was 57%.

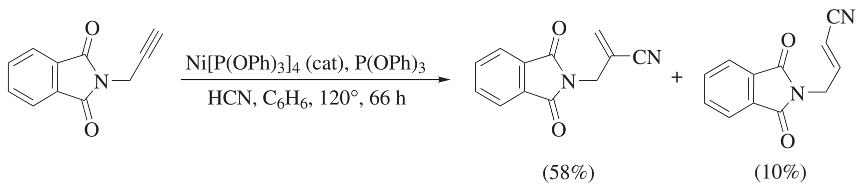


2-Cyano-4-methoxybut-1-ene and (*E*)-5-Methoxypent-2-enenitrile [Ni(0)-Catalyzed Hydrocyanation of an Alkynol Ether].[76] 4-Methoxybut-1-yne (0.84 g, 10 mmol), $Ni[P(OPh)_3]_4$ (0.23 g, 0.17 mmol), $P(OPh)_3$ (0.25 g, 0.65 mmol), HCN (0.4 mL, 10 mmol), and benzene (20 mL) were placed in a stainless-steel autoclave under nitrogen and heated at 120° for 18 hours. The benzene was removed and Kugelrohr distillation of the residue gave a mixture of nitriles as a clear liquid (0.8 g, 70% yield), bp 150° (oven temperature)/15 mmHg. 2-Cyano-4-methoxybut-1-ene: IR 2240 cm^{-1}; ^1H NMR (300 MHz) δ 2.5 (t, $J = 6.2$ Hz, 2 H), 3.55 (s, 3 H), 3.56 (t, $J = 6.2$ Hz, 2 H), 5.80 (s, 1 H), 5.91 (s, 1 H). (*E*)-5-Methoxypent-2-enenitrile: ^1H NMR (300 MHz) δ 2.50 (m, 2 H), 3.34 (s, 3 H), 3.49 (t, $J = 6.0$ Hz, 2 H), 5.43 (dt, $J = 16.3$, 1.8 Hz, 1 H), 6.74 (dt, $J = 16.4$, 6.8 Hz, 1 H); MS m/z: 111.

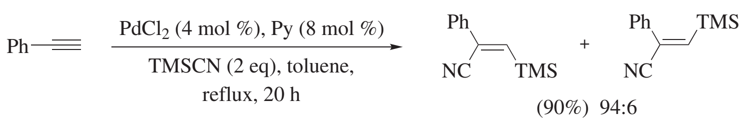


2-Ethyl-4-methylpenta-2,4-dienenitrile and 2-(1′-Methylethenyl)pent-2-enenitrile [Ni(0)-Catalyzed Hydrocyanation of an Enyne].[123] A mixture of 2-methylhex-1-en-3-yne (0.94 g, 10 mmol), $Ni[P(OPh)_3]_4$ (0.23 g, 0.18 mmol), $(PhO)_3P$ (0.15 mL, 0.57 mmol), HCN (0.39 mL, 10 mmol), and benzene

(20 mL) was placed in a stainless-steel autoclave under nitrogen, and heated at 120° for 18 hours. After removal of the benzene, Kugelrohr distillation gave the title nitriles as a colorless oil (0.5 g, 41% yield); bp 130° (oven temperature)/15 mmHg; IR 2225, 1620, 1595 cm^{-1}. The ratio of isomers determined by NMR spectroscopy was 90:10 2-ethyl-4-methylpenta-2,4-dienenitrile/2(1′-methylethenyl)pent-2-ene-nitrile. 2-Ethyl-4-methylpenta-2,4-dienenitrile: ^{1}H NMR (300 MHz) δ 1.19 (t, $J = 7.5$ Hz, 3 H), 1.92 (s, 3 H), 2.43 (dq, $J = 7.5$, 1.2 Hz, 2 H), 5.07 (s, 1 H), 5.23 (t, $J = 1.2$ Hz, 1 H), 6.62 (d, $J = 0.8$ Hz, 1 H); MS m/z: $[M]^+$ calcd for $C_8H_{11}N$, 121.0891; found, 121.089. 2-(1′-Methylethenyl)pent-2-ene-nitrile: ^{1}H NMR (300 MHz) δ 1.06 (t, $J = 7.5$ Hz, 3 H), 1.95 (d, 3 H), 2.34 (dq, $J = 7.5$ Hz, 2 H), 5.04 (s, 1 H), 5.23 (s, 1 H), 6.38 (t, $J = 7.6$ Hz, 1 H); MS m/z: 121.

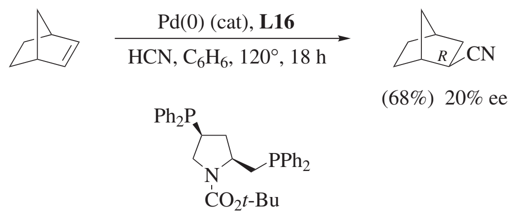


2-(2′-Cyanoprop-2′-enyl)phthalimide [Hydrocyanation of a Phtalimidomethylalkyne].[79] The substrate (5 mmol), $Ni[P(OPh)_3]_4$ (100 μmol), $P(OPh)_3$ (1 mmol), and dry degassed benzene (10 mL) were placed, in that order, in an autoclave under a nitrogen atmosphere. Hydrogen cyanide (5 mmol) was added using a gas-tight syringe. In some cases, when ambient temperature exceeded 20°, a larger volume of HCN was used. The reactor was sealed and heated at 120° for 66 hours. The autoclave was cooled, the excess hydrogen cyanide was vented, and the benzene was removed. The catalyst was precipitated with $CHCl_3$ and removed by filtration, and the solvent was removed in vacuo. Silica gel chromatography of the crude product (EtOAc/light petroleum) gave a mixture of the title compound and (E)-2-(3-cyanoprop-2-enyl)phthalimide in a ratio of 85:15 as a white solid (68% yield); mp 71–72°; ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.6, 116.6, 118.0, 123.8, 131.7, 132.9, 134.5, 167.1. The ^{1}H NMR spectral data were consistent with the literature.[77] Major isomer: mp 68–70°; IR 2230, 1780, 1720 cm^{-1}; ^{1}H NMR (300 Mz) δ 4.47 (t, $J = 1.3$ Hz, 2 H), 6.02 (t, $J = 1.3$ Hz, 1 H), 6.09 (t, $J = 1.3$ Hz, 1 H), 7.82 (m, 4 H). Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.9; H, 3.8; N, 13.2. Found: C, 67.9; H, 3.6; N, 13.1. Minor isomer: ^{1}H NMR (300 MHz) δ 4.44 (dd, $J = 5.5$, 1.8 Hz, 2 H), 5.52 (dt, $J = 16.3$, 1.8 Hz, 1 H), 6.73 (dt, $J = 16.3$, 5.5 Hz, 1 H), 7.82 (m, 4 H).



(Z)-2-Phenyl-3-(trimethylsilyl)prop-2-enenitrile [Addition of TMSCN to an Alkyne Catalyzed by $PdCl_2$/Pyridine].[80] To a solution containing phenylacetylene (0.55 mL, 5 mmol) and Me_3SiCN (1.34 mL, 10 mmol) in toluene

(10 mL) were added $PdCl_2$ (36 mg, 0.2 mmol) and pyridine (32 μL, 0.4 mmol). The mixture was heated at reflux under nitrogen with stirring for 20 hours. Monitoring of the reaction by GC showed that the reaction was complete within 10 hours. GC analysis of the reaction mixture showed the formation of 2-phenyl-3-(trimethylsilyl)prop-2-enenitrile in 93% yield (Z:E = 94:6). The solution was evaporated in vacuo, and the residue was chromatographed on silica gel [hexane/EtOAc (9:1)], followed by bulb-to-bulb distillation, to give the product mixture in 90% yield; bp 130–140° (25 mmHg); IR (neat) 3060, 2960, 2890, 2220 (CN), 1560 (C=C), 1490, 1450, 1250, 975, 860, 840, 755, 685 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.35 (s, 9 H, $SiCH_3$), 7.10 (s, 1 H, =CH), 7.37–7.41 (m, 2 H, Ph), 7.61–7.63 (m, 3 H, Ph); ^{13}C NMR ($CDCl_3$) δ −1.40 ($SiCH_3$), 117.9 (CN, $^3J_{CN-H}$ = 17 Hz), 125.7, 127.9, 128.9, 129.6, 135.1 (Ph, =C), 147.6 (=CH); MS m/z: [M^+] 201. Anal. Calcd for $C_{12}H_{15}NSi$: C, 71.59; H, 7.51; N, 6.96. Found: C, 71.84; H, 7.27; N, 6.99.

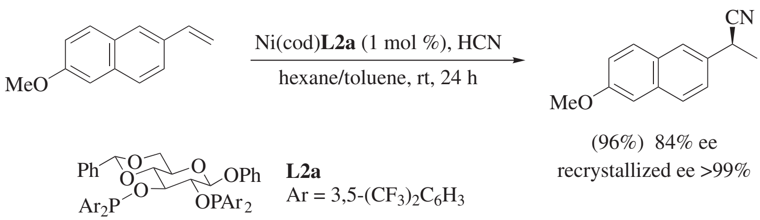


L16

(S,S)-BPPM

***exo*-(2*R*)-Cyanonorbornane [Pd-Catalyzed Asymmetric Hydrocyanation of a Strained Alkene].[48]** A Carius tube was charged with bis(dibenzylideneacetone)palladium (13.6 mg, 0.024 mmol), (2S, 4S)-*tert*-butoxycarbonyl-4-(diphenylphosphino)-2-((diphenylphosphino)methyl)pyrrolidine (**L16**, (S,S)-BPPM, 112 mg, 0.203 mmol), and a solution of bicyclo[2.2.l]heptene (2.68 g, 28.6 mmol) in benzene (5 mL). Hydrogen cyanide (385 mg, 14.3 mmol) was distilled into the tube, and a further addition of benzene (7 mL) was made. The tube was sealed under argon (500 mm Hg) and heated to 120° for 18 hours. Unreacted hydrogen cyanide, excess norbornene, and benzene were removed by distillation at atmospheric pressure, and the residue was distilled to yield a colorless oil, bp 80° (6 mmHg), which solidified to a colorless wax at room temperature [1.175 g, 68% yield (based on HCN)]; [α]$_D$ − 5.8° (c 0.9, $CHCl_3$). The product was confirmed to be pure bicyclo[2.2.1]heptane-*exo*-carbonitrile by GC (by comparison of the retention time to that of an authentic sample). Acid hydrolysis (6 M HCl, 110°, 3 hours) of the nitrile according to a published procedure[124] gave the corresponding acid as a colorless solid that was purified by sublimation (60°, 0.1 mmHg) to give bicyclo[2.2.l]heptene-*exo*-2-carboxylic acid (1.0 g) as a colorless solid; mp 57–58°; [α$_D$] −5.45 (c 1.0, EtOH). The enantiomeric purity of this acid was determined independently by ^{1}H NMR analysis of the (S)-methyl mandelate ester. To a solution of the *exo*-2-norbornanecarboxylic acid (140 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) at −10° was added (S)-methyl mandelate (183 mg,

1.1 mmol), 4-(dimethy1amino)pyridine (2.5 mg), and dicyclohexylcarbodiimide (206 mg, 1.0 mmol). After the mixture was stirred at $-10°$ for 3 hours, the dicyclohexylurea was removed by filtration, the solvent was removed under reduced pressure, and the residue was purified by preparative TLC [SiO_2, EtOAc/hexane (1:1)] to yield the desired ester as a homogeneous colorless oil; ^1H NMR (C_6D_6) δ 1.01−1.39 (6 H, m, H-5, H-6, H-7), 1.61 (1 H, dd, H-4), 2.09 (2 H, m, H-3), 2.38 (1 H, m, H-2), 2.54 + 2.87 (1 H, br s + br s, H-1), 3.19 (3 H, s, CO_2CH_3), 6.077 + 6.066 (1 H, s + s, CHOCO), 7.09 (3 H, m), 7.46 (2 H, d, *ortho* arom). Integration of the resonances at δ 6.077/6.061 and 2.87/2.54 ppm gave ratios of 60:40 and 40.5:59.5 (±l%), respectively, in agreement with the chiroptical data (20% ee). Hydrocyanations using (*R*)-BINAP [40% ee (*R*)], (*R*,*R*)-DIOP [86% yield, 9% ee (*R*)], and (*S*,*S*)-DIOP [13% ee (*S*)] ligands were carried out using similar procedures.

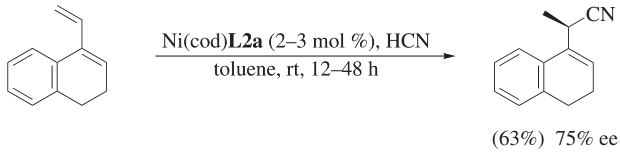


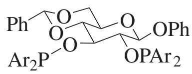
L2a
Ar = 3,5-$(CF_3)_2C_6H_3$

(96%) 84% ee
recrystallized ee >99%

(*S*)-2-(6-Methoxy-2-naphthalene)propionitrile [Asymmetric Hydrocyanation of a Vinylarene].[45] To a solution of $Ni(cod)_2$ (0.059 g, 0.22 mmol) and the ligand **L2a** (0.271 g, 0.22 mmol) in 10 mL of hexane were added 6-methoxy-2-vinylnaphthalene (4.00 g, 21.7 mmol) and 110 mL of hexane. An approximately 2 M solution of HCN in toluene (11 mL, 22 mmol) was added to the resulting slurry by addition funnel over 2.5 hours. The initially heterogeneous solution became an orange-brown homogeneous solution about half-way through the addition, and then the product precipitated as a white powder. GC analysis showed an 84% conversion at the end of the addition; therefore, an additional 3 mL of the HCN solution was added over 1 hour. After the reaction mixture was stirred overnight, benzene was added to dissolve all of the solids. GC analysis showed >99% conversion. HPLC analysis of a small sample isolated by silica gel chromatography (hexane/Et_2O 90:10) showed 84% ee. The solids that precipitated initially were enriched up to 93% ee. Recrystallization provided optically pure nitrile. After concentration of the reaction mixture in vacuo, the remaining solids were slurried in 200 mL of hexane and collected by filtration, affording 3.555 g of an off-white solid. The filtrate was concentrated in vacuo to about 50 mL, and a second crop of product was isolated by filtration (yield 0.468 g). A third crop of product was then isolated by silica gel chromatography of the filtrate (90:10 hexane/Et_2O), yield 0.380 g. The total yield was 4.403 g (96%). Two recrystallizations from 10% Et_2O/hexanes afforded pure product in greater than 99% ee as judged by HPLC analysis on a Chiralcel OJ column using hexane/2-propanol (90:10) as eluent; mp 99 −100°; $[\alpha]_D$ -29.4 ± 0.8 (*c* 1, $CHCl_3$); ^1H

NMR ($CDCl_3$) δ 1.70 (d, $J = 7$ Hz, 3 H), 3.92 (s, 3 H), 4.00–4.04 (q, $J = 7$ Hz, 1 H), 7.14 (d, $J = 2.6$ Hz, 1 H), 7.19 (dd, $J = 9.1$, 2.6 Hz, 1 H), 7.39 (m, 1 H), 7.72–7.77 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 21.4, 31.2, 55.3, 105.6, 119.5, 121.7, 124.9, 125.3, 127.9, 128.7, 129.3, 132.0, 134.0, 158.1.





L2a
Ar = 3,5-$(CF_3)_2C_6H_3$

(*R*)-2-(3,4-Dihydro-1-naphthalene)propionitrile [Asymmetric Hydrocyanation of a 1,3-Diene].[53] To a mixture of the phosphinite ligand **L2a** (2.1 mol%) and $Ni(cod)_2$ (2 mol%) in a drybox was added 0.2 mL of toluene, and the mixture was stirred for 5 minutes at room temperature. To this solution a 0.2-mL toluene solution of the diene (0.5 mmol) was added dropwise. The solution turned brown, and the mixture was stirred for 10 minutes at room temperature. Then 0.14 mL of 2 M HCN in toluene was added slowly, dropwise, and the reaction was stirred for another 12 hours. Additional $Ni(cod)_2$ (1 mol %) and 2 M HCN in toluene (0.1 mL) were added, respectively, and the reaction mixture was stirred for an additional 12 to 48 hours. The reaction flask was removed from the drybox and N_2 gas was passed into the reaction mixture in a well-ventilated hood to remove any excess HCN. On a larger scale, the HCN/N_2 effluent should be trapped in a solid KOH tower. The crude mixture was passed through a small pad of silica to remove the catalyst. The solvent was removed under vacuum and the product was further purified by short silica gel column chromatography using a gradient of 100% hexane to hexane/Et_2O (19:1) to afford the pure product (63% yield). The enantiomeric ratio of the final product was determined by HPLC on a Chiralcel OJ column (hexanes/2-propanol 95:5, 0.5 mL/min, 254 nm, t_R 20.53 min, t_R 23.62 min; 75% ee); $[\alpha]^{20}_D$ −61° (*c* 0.18, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.6 (d, $J = 7.5$ Hz, 3 H), 2.35–2.39 (m, 2 H), 2.79 (t, $J = 8$ Hz, 2 H), 3.92 (q, $J = 7$ Hz, 1 H), 6.36 (t, $J = 4.5$ Hz, 1 H), 7.20–7.28 (m, 4 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.9, 22.9, 27.9, 28.0, 121.7, 121.8, 126.6, 127.2, 127.6, 128.2, 131.8, 132.7, 136.9. The configuration was established by comparison of the optical rotation of the fully aromatic derivative (prepared by reaction of the product with DDQ in benzene) with that of an authentic sample.

TABULAR SURVEY

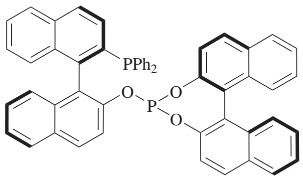
The literature up to the end of 2008 is included in the Tabular Survey. Tables are classified according to type of substrates except for the section on asymmetric hydrocyanations, which is dealt with separately. Table 1 presents the substrates that are not described by Tables 2–4. In all tables and sub-tables the substrates are

organized in the order of increasing carbon count. Under the heading 'conditions' the best available set of parameters to carry out the transformation that is available in open literature is provided. In many instances, more optimized conditions may be available in the patent literature, which should be consulted for specific compounds. It should be noted that the complex $Pd(DIOP)_2$ or $Ni(DIOP)_2$ and the corresponding ligand have opposite optical rotations, e.g., (−)-DIOP forms (+)-$Pd(DIOP)_2$ and (+)-$Ni(DIOP)_2$, respectively.

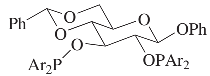
The following abbreviations are used in the tables:

Ac	acetyl
All	allyl
cod	1,5-cyclooctadiene
conv.	conversion
dba	dibenzylideneacetone
DEIPS	diethylisopropylsilyl
DIBALH	diisobutylaluminum hydride
Dppp	1,3-bis(diphenylphosphino)propane
EG	ethylene glycol
MCPBA	*m*-chloroperoxybenzoic acid
Pht	*N*-phthalimidoyl
Rac	racemic
TBS	*tert*-butyldimethylsilyl
TEA	triethylamine
TES	triethylsilyl
TMS	trimethylsilyl
TOF	turnover frequency
tol	tolyl, methylphenyl
TON	turnover number

CHART 1. LIGANDS FOR METAL-CATALYZED HYDROCYANATION OF ALKENES

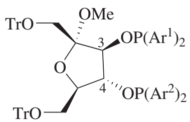


L1
(R,S)-BINAPHOS



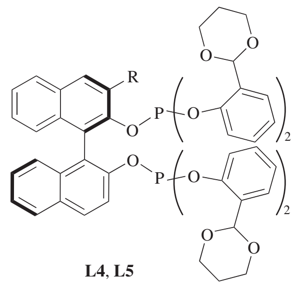
L2

	Ar
2a	3,5-$(CF_3)_2C_6H_3$
2b	3,5-$F_2C_6H_3$
2c	C_6H_5
2d	3,5-$Me_2C_6H_3$



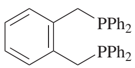
L3

	Ar^1	Ar^2
3a	3,5-$(CF_3)_2C_6H_3$	3,5-$(CF_3)_2C_6H_3$
3b	Ph	Ph
3c	3,5-$(CF_3)_2C_6H_3$	Ph
3d	Ph	3,5-$(CF_3)_2C_6H_3$

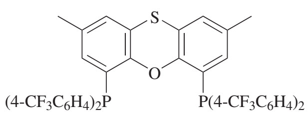


L4, **L5**

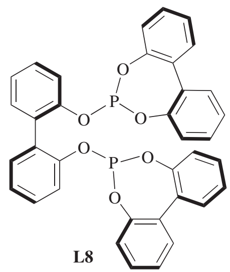
	R
4	H
5	Me



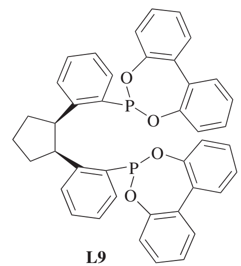
L6
phmep



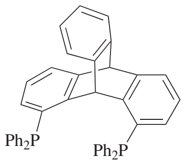
L7
CF_3-thiaxantphos



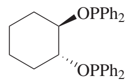
L8



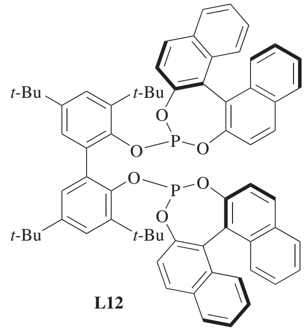
L9



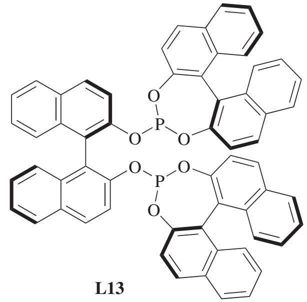
L10



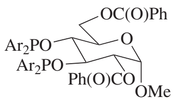
L11 (racemic)



L12

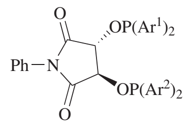


L13



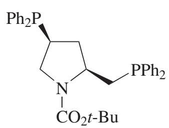
L14

	Ar
14a	3,5-$(CF_3)_2C_6H_3$
14b	Ph
14c	3,5-$Me_2C_6H_3$



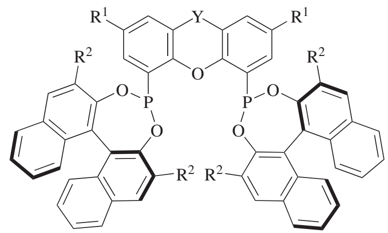
L15

	Ar^1	Ar^2
15a	3,5-$(CF_3)_2C_6H_3$	3,5-$(CF_3)_2C_6H_3$
15b	Ph	Ph
15c	Ph	3,5-$(CF_3)_2C_6H_3$



L16

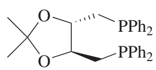
(*S*,*S*)-BPPM



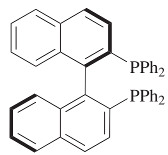
L17

	Y	R^1	R^2
17a	CMe_2	H	H
17b	S	Me	H
17c	S	Me	Me

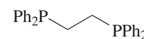
CHART 1. LIGANDS FOR METAL-CATALYZED HYDROCYANATION OF ALKENES (*Continued*)



(*S*,*S*)-(+)-DIOP



(*R*)-BINAP



diphos

TABLE 1. HYDROCYANATION OF ALKENES

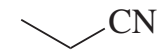
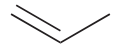
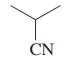
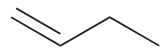
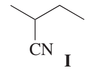
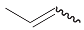
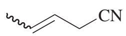
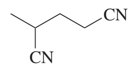
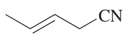
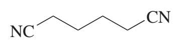
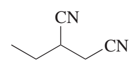
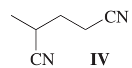
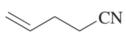
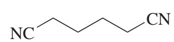
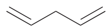
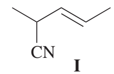
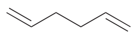
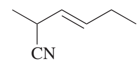
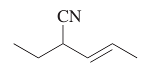
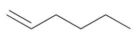
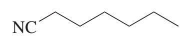
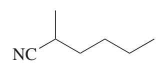
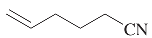
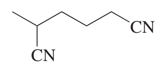
	Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2		$Co_2(CO)_8$	Alkene (excess), cat (17 g), HCN (27 g), sealed vessel (200 psi), 130°, 7 h	 63% conv.	36
C_3		$Co_2(CO)_8$	Alkene (150 g), cat (17 g), HCN (14 g), sealed vessel (110 psi), 130°, 15 h	 65% conv.	36
C_4		$Co_2(CO)_8$	Alkene (56 g), cat (17g), HCN (14 g), sealed vessel (40 psi), 130°, 8 h	 **I** 67% conv.	36
		$Co_2(CO)_8$	Alkene (56 g), cat (17g), HCN (14 g), sealed vessel (32 psi), 130°, 8 h	**I** 9% conv.	36
		$Co_2(CO)_8$	Alkene (56 g), cat (17g), Ph_3P (8.5 g), HCN (14 g), sealed vessel (39 psi), 130°, 8 h	**I** 24% conv.	36
C_5		$Co_2(CO)_8$	Alkene (40.5 g), cat (17 g), HCN (27 g), 130°, 14.5 h	 7% conv.	36
	 **I**	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (2.49 mmol), cat (8.3 mmol), $ZnCl_2$ (2 mmol), HCN, 68°	 **II** +  **III** +  **IV** + isomers of **IV** **II** + **III** + **IV** + **V** (~100), **II**:**III**:**IV**:**V** = 35:7:1:39	21, 16
		$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (1.02 mmol), cat (2 mmol), $P(O\text{-}4\text{-}tol)_3$ (7.8 mmol), $Ph_3Sn^+TsO^-$ (0.18 mmol), HCN (excess), 50°	**II** + **IV** (~100), **II**:**IV** = 91.4:7.4	60
		$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (0.2 mmol), cat (0.05 mmol), Ph_3B (0.05 mmol), HCN (0.2 mmol), rt	 (98)	21

TABLE 1. HYDROCYANATION OF ALKENES (*Continued*)

Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (100 mmol), cat (1 mmol), $P(O\text{-}4\text{-}tol)_3$ (16 mmol), HCN (100 mmol), 90°, 1.5 h	 **I** (81), 82% conv.	42
	Ni[(–)-DIOP]$_2$ [a]	Alkene (390 mmol), cat (1 mmol), (–)-DIOP (6.3 mmol), HCN (275 mmol), 90°, 1.5 h	**I** (74)	63
	Ni(**L6**)$_2$	Alkene (50 mmol), cat (1 mmol), **L6** (6.3 mmol), acetone cyanohydrin (100 mmol), 90°, 1.5 h	**I** (63)	63
C_6 	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (100 mmol), cat (1 mmol), $P(O\text{-}4\text{-}tol)_3$ (16 mmol), HCN (100 mmol), 90°, 1.5 h	 **I** (36) +  **II** (43)	42
	Ni[(–)-DIOP]$_2$ [a]	Alkene (390 mmol), cat (1 mmol), (–)-DIOP (6.3 mmol), HCN (275 mmol), 90°, 1.5 h	**I** (38) + **II** (45)	63
	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (200 mmol), cat (1 mmol), $P(O\text{-}4\text{-}tol)_3$ (5 mmol), $ZnCl_2$ (2 mmol), HCN (added slowly), MeCN (25 mL), 60°, 2.5 h	 (20) +  (5)	40
	$Co_2(CO)_8$	Alkene (19 g), cat (17 g), HCN (14 g), 130°, 8 h	 36% conv.	36

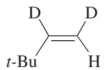
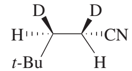
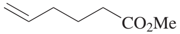
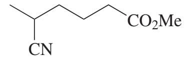
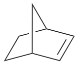
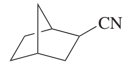
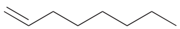
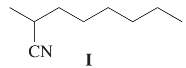
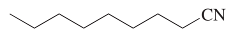
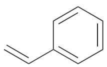
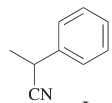
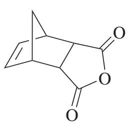
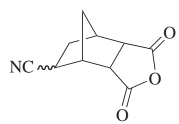
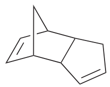
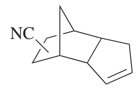
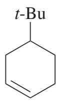
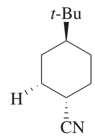
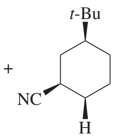
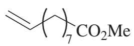
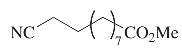
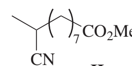
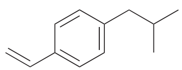
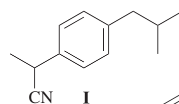
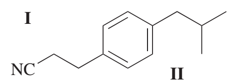
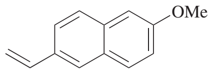
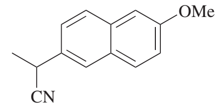
	Pd[(–)-DIOP]$_2$ [a]	cat (0.3 mol %), HCN, 120°, 18 h	 (10)	125, 44
C_7 	$Co_2(CO)_8$	Alkene (22 g), cat (17 g), HCN (27 g), sealed vessel (28 psi), 130°, 8 h	 19% conv.	36
	Pd[P(OPh)$_3$]$_4$	Alkene (1.24 M), cat (0.01 M), P(OPh)$_3$ (1.1 M), HCN (0.66 M)	 **I** (83)	59, 47
	Ni[P(OPh)$_3$]$_4$	Alkene (64 mmol), cat (0.09 mmol), P(OPh)$_3$ (0.6 mmol), HCN (82 mmol), C_6H_6	**I** (80)	47
	Pd(diphos)$_2$	Various conditions	**I** (—)	47
C_8 	$Co_2(CO)_8$	Alkene (56 g), cat (17 g), Ph_3P (8.5 g), HCN (27 g), sealed vessel (46 psi), 130°, 8 h	 **I** 24% conv.	36
	Ni(cod)$_2$	Alkene/cat/**L7**/$AlCl_3$/HCN (20:1:1.05:1:25), toluene, 60°	 (49) + **I** (2)	126
	$Co_2(CO)_8$	Alkene (104 g), cat (17 g), hydroquinone (2 g), HCN (14 g), sealed vessel (25 psi), 130°, 8 h	 **I** 52% conv.	36
	Ni(cod)$_2$ + **L7**	Alkene (1.3 mmol), Ni(cod)$_2$ (0.065 mmol), **L7** (0.065 mmol), HCN (excess), toluene (2 mL), 60°, 16 h	**I** (90)	65
C_9 	$Co_2(CO)_8$	Alkene (164 g), cat (68 g), Ph_3P (20 g), HCN (54 g), 130°, 8 h	 28% conv.[b]	36

TABLE 1. HYDROCYANATION OF ALKENES (*Continued*)

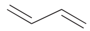
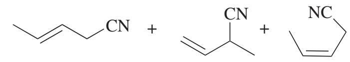
Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	$Co_2(CO)_8$	Alkene (60 g), cat (17 g), PPh_3 (8.5 g), HCN (14 g), 130°, 15.5 h	 24% conv.[b]	36
	$Ni[P(OPh)_3]_4$	Alkene (65 mmol), cat (2.1 mmol), $P(OPh)_3$ (9.7 mmol), $ZnCl_2$ (4 mmol), HCN (50 mmol), toluene, 60°	 (5) +  (10)	44
C_{11} 	$Ni(cod)_2$	Alkene/cat/**L7**/$AlCl_3$/HCN (20:1:1.05:1:25), toluene, 60°	 **I** +  **II** **I** + **II** (36), **I**:**II** = 75:25	126
C_{12} 	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (21.5 mmol), cat (1.0 mmol), $P(O\text{-}4\text{-}tol)_3$ (1.0 mmol), $ZnCl_2$ (0.35 mmol), HCN (excess), 88°, 3 h	 **I** +  **II** **I** + **II** (68), **I**:**II** = 90:10	43

C_{13} 	$Ni[P(O\text{-}4\text{-}tol)_3]_4$	Alkene (15.6 mmol), cat (1.0 mmol), $P(O\text{-}4\text{-}tol)_3$ (1.0 mmol), HCN (excess), toluene (15 mL)		(93)	43

[a] The complex $Pd(DIOP)_2$ or $Ni(DIOP)_2$ and the corresponding ligand have opposite optical rotations.

[b] The position of the nitrile is unknown.

TABLE 2. HYDROCYANATION OF 1,3-DIENES

Diene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	CuBr	Diene (52 mmol), cat (2.5 mmol), Cl_3CCO_2H (3 mmol), HCN (107 mmol), MeCN, 79°, 16 h	 **I** (68) **II** (4) (3)	66, 67
	$Ni[P(OPh)_3]_4$	Diene (100 mmol), cat (1 mmol), $P(OPh)_3$ (16 mmol), HCN (100 mmol), 90°, 90 min	**I** (64) + **II** (34)	42
	$Ni[P(OPh)_3]_4$	Diene (410 mmol), cat (1 mmol), $P(OPh)_3$ (14 mmol), hydroquinone (2 mmol), HCN (180 mmol), 90°, 90 min	**I** (68) + **II** (20)	63
	$Ni(cod)_2$ + **L9**	HCN/diene (3:4), **L9**/Ni (21:20), Ni (0.1 mol %), 120°, 3 h	**I** (45) + **II** (37), TON 644, TOF 215	68
	$Ni(cod)_2$ + $P(O\text{-}4\text{-}tol)_3$	HCN/diene (3:4), $P(O\text{-}4\text{-}tol)_3$/Ni (6:1), Ni (0.2 mol %), 120°, 3 h	**I** (5) + **II** (3), TON 30, TOF 10	68
	$Ni(cod)_2$ + **L10**	Diene (2.25 mmol), $Ni(cod)_2$ (0.018 mmol), **L10** (0.018 mmol), acetone cyanohydrin (2.7 mmol), solvent (2 mL), 90°, 5 h	**I** + **II** Solvent / **I** / **II** dioxane (81) (4) toluene (31) (17)	27
	$Ni(cod)_2$ + **L10**	Diene (2.25 mmol), $Ni(cod)_2$ (0.018 mmol), **L10** (0.018 mmol), HCN (excess), dioxane (2 mL), 90°, 5 h	**I** (93) + **II** (2)	27
	Ni(**L8**)$_2$	Diene (46 mmol), cat (0.088 mmol), acetone cyanohydrin (34 mmol), 140°, 18 h	**I** (35) + **II** (29)	61

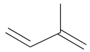
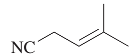
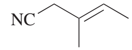
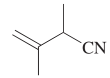
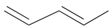
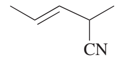
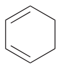
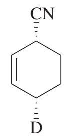
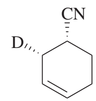
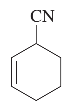
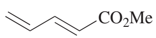
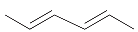
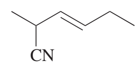
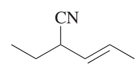
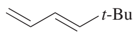
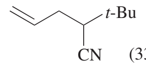
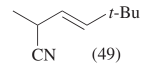
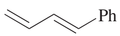
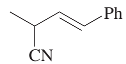
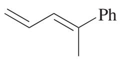
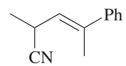
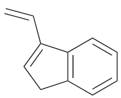
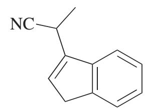
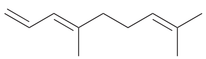
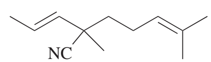
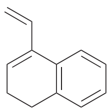
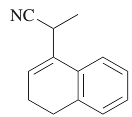
C_5 	CuBr	Diene (52 mmol), cat (2.5 mmol), Cl_3CCO_2H (3 mmol), HCN (107 mmol), MeCN, 79°, 16 h	 (39) + oligomers	66, 67
	$Ni[P(OPh)_3]_4$	Diene (100 mmol), cat (1 mmol), $P(OPh)_3$ (16 mmol), HCN (100 mmol), 90°, 90 min	 (15) +  (11)	42
	CuBr	Diene (52 mmol), cat (2.5 mmol), Cl_3CCO_2H (3 mmol), HCN (107 mmol), MeCN, 79°, 16 h	 **I** (12) + oligomers	66, 67
	$Ni[P(OPh)_3]_4$	Diene (100 mmol), cat (1 mmol), $P(OPh)_3$ (16 mmol), HCN (100 mmol), 90°, 90 min	**I** (74)	42
C_6 	$Ni[P(OPh)_3]_4$	Diene (3 mmol), cat (0.06 mmol), $P(OPh)_3$ (0.18 mmol), DCN (3 mmol), MeCN, 60°, 2 h	 **I** +  **II** **I** + **II** (38), **I**:**II** = 1:1[a]	23
	$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (5 mol %), **L11** (5 mol %), toluene, rt, 20 h	 (>95)	53
	$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (5 mol %), **L11** (5 mol %), toluene, rt, 20 h	no reaction	53
	$Ni[(–)\text{-}DIOP]_2$ [b]	Diene (390 mmol), cat (1 mmol), DIOP (6.3 mmol), HCN (275 mmol), 90°, 1.5 h	 (17) +  (16)	63

TABLE 2. HYDROCYANATION OF 1,3-DIENES (*Continued*)

	Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (10 mol %), **L11** (10 mol %), toluene, 50°, 20 h	 (33) +  (49)	53
C_{10}		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (10 mol %), **L11** (10 mol %), toluene, rt, 20 h	 (87)	53
C_{11}		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (10 mol %), **L11** (10 mol %), toluene, 50°, 24 h	 (32)	53
		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (5 mol %), **L11** (5 mol %), toluene, rt, 48 h	 (71)	53
		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (10 mol %), **L11** (10 mol %), toluene, 50°, 24 h	 (83)	53
C_{12}		$Ni(cod)_2$ + **L11**	Diene/HCN (1:1), $Ni(cod)_2$ (10 mol %), **L11** (10 mol %), toluene, rt, 24 h	 (80)	53

[a] Deuterio-1,3-cyclohexadiene is not formed.

[b] The complex $Pd(DIOP)_2$ or $Ni(DIOP)_2$ and the corresponding ligand have opposite optical rotations.

TABLE 3A. HYDROCYANATION OF ALKYNES USING HCN

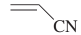
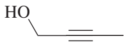
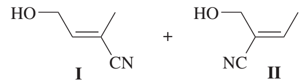
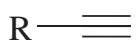
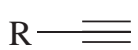
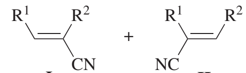
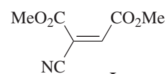
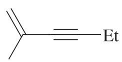
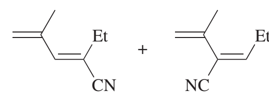
Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2 	$CuCl_2$, NH_4Cl, $AlCl_3$	Alkyne/HCN (10:1), 70–90°	 (80–90)	7
C_4 	$Ni[P(OPh)_3]_4$	Alkyne (5 mmol), cat (0.2 mmol), $P(OPh)_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 60°, 20 h	 **I + II** (62), **I**:**II** = 55:45	75
	$Ni(\mathbf{L6})_2$	Alkyne (5 mmol), cat (0.1 mmol), **L6** (0.7 mmol), HCN (5.2 mmol), C_6H_6 (20 mL), 60°, 18 h	**I + II** (72), **I**:**II** = 50:50	75
C_{5-8} 	$Ni[P(OPh)_3]_4$	Alkyne (21 mmol), cat (0.54 mmol), $P(OPh)_3$ (2.4 mmol), $ZnCl_2$ (1 mmol), HCN (32 mmol in 5 mL toluene), 60°, 10 h		
R			**I + II** / **I:II**	
n-Pr			(40) 1:19	72
n-Bu			(33) 1:24	72, 71
t-Bu			(45) 4:1	72, 71
n-C_6H_{13}			(45) 2:23	72, 71
Ph			(35) 17:3	72, 71
C_{5-11} 	$Ni[P(OPh)_3]_4$	Alkyne (39 mmol), cat (0.2 mmol), $P(OPh)_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	**I + II**	
R			**I + II** / **I:II**	
n-Pr			(60) 13:87	72
n-Bu			(73) 14:86	72, 71
t-Bu			(15) 88:12	72, 71
n-C_6H_{13}			(60) 14:86	72, 71
Ph			(48) 98:2	72, 71
$PhCH_2OCH_2CH_2$			(78) 15:85	76

TABLE 3A. HYDROCYANATION OF ALKYNES USING HCN (*Continued*)

Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-24} R^1—≡—R^2	$Ni[P(OPh)_3]_4$	Alkyne (39 mmol), cat, $P(OPh)_3$ (2.5 mmol), cyanide source (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	 **I** + **II**	73, 74

R^1	R^2	Cyanide Source	Alkyne/Cat	**I + II**	**I:II**
TMS	H	acetone cyanohydrin	195:1	(74)	1:3
TMS	Me	acetone cyanohydrin	195:1	(90)	4:1
TMS	Me	acetone cyanohydrin	45:1[a]	(87)	4:1
TBS	H	HCN	45:1	(57)	7:13
TBS	Me	HCN	45:1	(88)	49:1
TMS	*n*-Bu	acetone cyanohydrin	90:1[a]	(90)	18:7
TMS	Ph	HCN	90:1	(80)	1:4
TBS	Ph	HCN	45:1	(74)	9:1
Ph_3Si	*n*-Bu	HCN	18:1[b]	(75)	1:0

Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 MeO_2C—≡—CO_2Me	$Ni[P(OPh)_3]_4$	Alkyne (39 mmol), cat (0.2 mmol), $P(OPh)_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	 **I** (27)	72, 71
		Alkyne (21 mmol), cat (0.54 mmol), $P(OPh)_3$ (2.4 mmol), $ZnCl_2$ (1 mmol), HCN (32 mmol in 5 mL toluene), 60°, 10 h	**I** (5)	72, 71
C_7 	$Ni[P(OPh)_3]_4$	Alkyne (39 mmol), cat (0.2 mmol), $P(OPh)_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	 **I** + **II**; **I + II** (41), **I**:**II** = 2:3	123

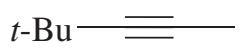
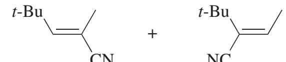
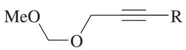
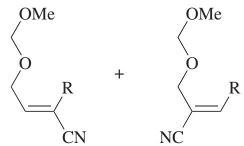
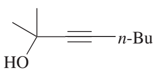
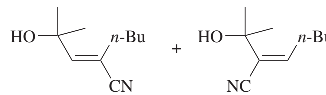
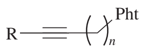
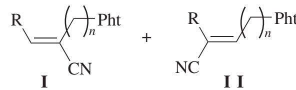
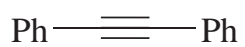
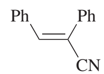
	Ni[P(OPh)$_3$]$_4$	Alkyne (21 mmol), cat (0.54 mmol), P(OPh)$_3$ (2.4 mmol), $ZnCl_2$ (1 mmol), HCN (32 mmol in 5 mL toluene), 60°, 10 h	 **I** **II** **I** + **II** (78), **I**:**II** = 9:1	72, 71
C_{7-11}				
	Ni[P(OPh)$_3$]$_4$	Alkyne (39 mmol), cat (0.2 mmol), P(OPh)$_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	 **I** **II**	76
R			**I** + **II** **I**:**II**	
CH_2OMe			(71) 1:1	
n-Bu			(90) 1:1	
Ph			(61) 1:3	
C_9 	Ni[P(OPh)$_3$]$_4$	Alkyne (5 mmol), cat (0.2 mmol), P(OPh)$_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 60°, 20 h	 **I** **II** **I** + **II** (84), **I**:**II** = 50:50	75
	Ni(**L6**)$_2$	Alkyne (5 mmol), cat (0.1 mmol), **L6** (0.7 mmol), HCN (5.2 mmol), C_6H_6 (20 mL), 120°, 18 h	**I** + **II** (79), **I**:**II** = 75:25	75

TABLE 3A. HYDROCYANATION OF ALKYNES USING HCN (*Continued*)

Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-17}				
	Ni[P(OPh)$_3$]$_4$	Alkyne (39 mmol), cat (0.2 mmol), P(OPh)$_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°	 I + II	78, 77
R / *n*		Time (h)	I + II / I:II	
H / 1		66	(88) / 4:1	
H / 2		20	(88) / 9:1	
Me / 1		20	(72) / 1:1	
Ph / 1		20	(76) / 9:1	
C_{14}				
	Ni[P(OPh)$_3$]$_4$	Alkyne (39 mmol), cat (0.9 mmol), P(OPh)$_3$ (2.5 mmol), HCN (32 mmol), C_6H_6 (25 mL), autoclave, 120°, 20 h	 I (93)	72, 71
	Ni[P(OPh)$_3$]$_4$	Alkyne (21 mmol), cat (0.54 mmol), P(OPh)$_3$ (2.4 mmol), $ZnCl_2$ (1 mmol), HCN (32 mmol in 5 mL toluene), 60°, 10 h	**I** (82)	72, 71

[a] The reaction is performed in toluene and without autoclave.

[b] This substrate requires 72 h reaction time.

TABLE 3B. HYDROCYANATION OF ALKYNES USING TMSCN

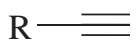
Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-12}				
	$PdCl_2$		 I + II	80
R			I + II / I:II	
$NCCH_2CH_2$		Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	(63) 84:16	
$AcOCH_2CH_2$		Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	(36) 80:20	
$TMSOCH_2CH_2$		Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	(34) 88:12	
Ph		Alkyne (5 mmol), cat (0.2 mmol), pyridine (0.4 mmol), TMSCN (10 mmol), toluene (10 mL), reflux, 10 h	(90) 95:5	
n-C_6H_{13}		Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	(41) 85:15	
2-naphthalene		Alkyne (5 mmol), cat (0.2 mmol), pyridine (0.4 mmol), TMSCN (10 mmol), toluene (10 mL), reflux, 10 h	(90) 95:5	

TABLE 3B. HYDROCYANATION OF ALKYNES USING TMSCN (*Continued*)

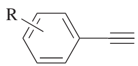
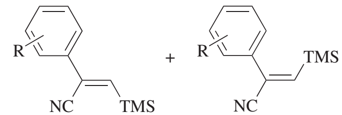
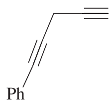
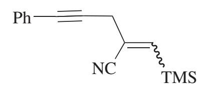
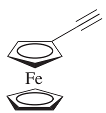
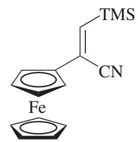
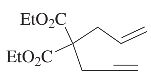
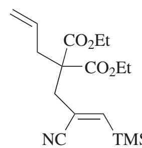
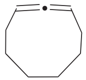
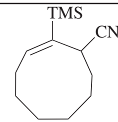
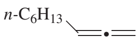
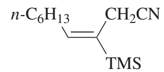
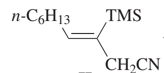
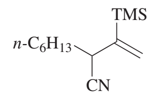
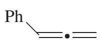
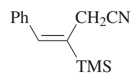
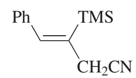
Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-9} 	$PdCl_2$	Alkyne (5 mmol), cat (0.2 mmol), pyridine (0.4 mmol), TMSCN (10 mmol), toluene (10 mL), reflux, 10 h	 **I** + **II** R / **I** + **II** / **I**:**II** 4-F (38) — 4-Cl (47) 94:6 2-Cl (23) 81:19 2-OMe (85) 83:17 4-OMe (90) 95:5	80
C_{11} 	$PdCl_2$	Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	 (47), *Z*:*E* = 87:13	80
C_{12} 	$PdCl_2$	Alkyne (5 mmol), cat (0.2 mmol), pyridine (0.4 mmol), TMSCN (10 mmol), toluene (10 mL), reflux, 10 h	 (52)	80
C_{13} 	$PdCl_2$	Alkyne (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 10 h	 (36)	80

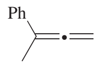
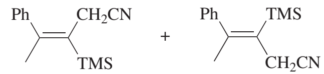
TABLE 3C. HYDROCYANATION OF ALLENES USING TMSCN

Allene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	$PdCl_2$	Allene (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 20 h	 (54) **I**	81
	$NiCl_2$, DIBALH	—	**I** (78)	80
	Pd or Ni salt	Allene (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 20 h	 **I** +  **II** +  **III** (3–20%)	81
	Pd or Ni salt	Allene (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 20 h	 **I** +  **II**	81

Cat	**I + II**	**I:II**
$PdCl_2$	(70)	89:11
$PdCl_2$, pyridine	(66)	95:5
$PdBr_2$, pyridine	(87)	89:11
$NiCl_2$, DIBALH	(54)	72:28

Cat	**I + II**	**I:II**
$PdCl_2$, pyridine	(67)	88:12
$PdBr_2$, pyridine	(75)	89:11
$NiCl_2$, DIBALH	(48)	54:46

TABLE 3C. HYDROCYANATION OF ALLENES USING TMSCN (*Continued*)

Allene	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	Pd or Ni salt	Allene (2.5 mmol), cat (0.1 mmol), pyridine (0.2 mmol), TMSCN (5 mmol), toluene (5 mL), reflux, 20 h	 **I** + **II**	81

Cat	**I** + **II**	**I**:**II**[a]
$PdBr_2$, pyridine	(60)	67:33
$NiCl_2$, DIBALH	(58)	64:36

[a] The product configuration assignment is tentative.

TABLE 3D. HYDROCYANATION OF ALKYNES USING CYANOMETALLATES

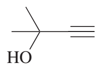
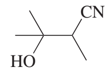
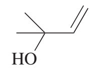
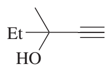
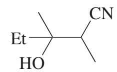
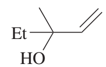
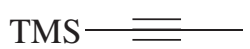
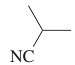
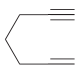
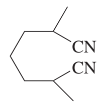
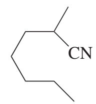
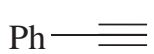
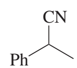
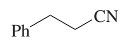
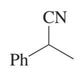
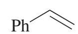
Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	$K_2[Ni(CN)_4]$	Alkyne/cat (2:1), $K_2[Ni(CN)_4]$/$NaBH_4$ (4 mmol), H_2O, 45°, 4 h	 (49) +  (12)	31
C_6 	$K_2[Ni(CN)_4]$	Alkyne/cat (2:1), $K_2[Ni(CN)_4]$/$NaBH_4$ (4 mmol), H_2O, 45°, 4 h	 (59) +  (10)	31
	$K_2[Ni(CN)_4]$	Alkyne/cat (2:1), $K_2[Ni(CN)_4]$/$NaBH_4$ (4 mmol), H_2O, 45°, 8 h	 (92)	31
C_7 	$K_2[Ni(CN)_4]$	$K_2[Ni(CN)_4]$/$NaBH_4$ (4 mmol), EG, 45°, 6 h	 (76) +  (5) **I** **II**	31
	$K_2[Ni(CN)_4]$	$K_2[Ni(CN)_4]$/Zn (4 mmol), H_2O, 45°, 6 h	**I** (28) + **II** (53)	31
C_8 	$K_2[Ni(CN)_4]$	Alkyne/cat/$NaBH_4$/KCN (8:1:5:10), H_2O/EG (9:1), 9 h	 +  **I** **II** **I** + **II** (90), **I**:**II** = 97:3	31
	$K_2[Ni(CN)_4]$	Alkyne/cat/Zn/KCN (2:1:5:2), H_2O, 2 h	 +  **I** **III** **I** + **III** (95), **I**:**III** = 93:7	31

TABLE 3D. HYDROCYANATION OF ALKYNES USING CYANOMETALLATES (*Continued*)

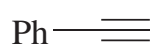
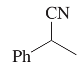
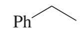
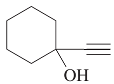
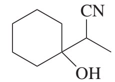
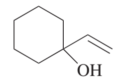
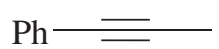
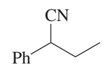
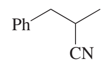
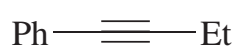
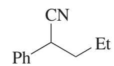
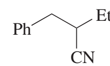
Alkyne	Catalyst	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	$K_3[Co(CN)_5]$	Alkyne (5 mmol), alkyne/cat (1:1), $CoCl_2$ (5 mmol), KCN (24.5 mmol), H_2O (25 mL), 45°, 24 h	 (18) +  (2)	82
	$K_3[Co(CN)_5]$	Alkyne (5 mmol), alkyne/cat (1:1), $CoCl_2$ (5 mmol), KCN (24.5 mmol), H_2O (25 mL), 45°, 10 h	 **I** (71) +  **II** (13)	82
	$K_2[Ni(CN)_4]$	Alkyne (8 mmol), $K_2[Ni(CN)_4]$/ $NaBH_4$ (4 mmol), H_2O, 45°, 4 h	**I** (77) + **II** (14)	31
C_9				
	$K_2[Ni(CN)_4]$	Alkyne (8 mmol), $K_2[Ni(CN)_4]$/ $NaBH_4$ (4 mmol), H_2O/EG, 45°, 4 h	 (40) +  (23)	31
C_{10}				
	$K_2[Ni(CN)_4]$	Alkyne (8 mmol), $K_2[Ni(CN)_4]$/ $NaBH_4$ (4 mmol), H_2O/EG, 45°, 8 h	 (43) +  (28)	31

TABLE 4A. ASYMMETRIC HYDROCYANATION OF MONOENES AND 1,3-DIENES

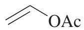
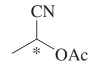
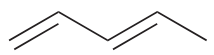
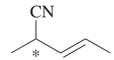
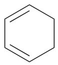
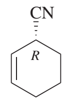
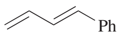
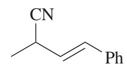
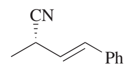
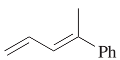
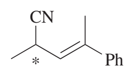
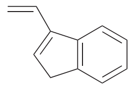
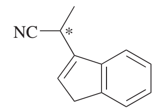
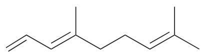
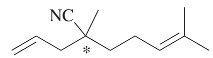
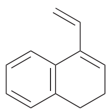
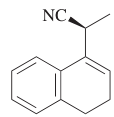
Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_4 	$Ni(cod)_2$ + **L12**	Alkene/$Ni(cod)_2$/**L12**/acetone cyanohydrin (100:1:7:110), toluene, 100°, 24 h	 24% conv., 83% selectivity,[a] 73% ee[b]	51
C_5 	$Ni(cod)_2$ + **L5**	Alkene/$Ni(cod)_2$/**L5**/HCN (100:1:1.1:200), toluene (1.2 mL), 60°, 4 h	 (100), 33[b]	87
C_6 	$Ni(cod)_2$ + **L4** or **L5**	Alkene/$Ni(cod)_2$/**L**/HCN (100:1:1.1:200), toluene (1.2 mL), 4 h	 Ligand / Temp (°) **L4** 80 (100), 43 **L5** 80 (100), 63 **L5** 0 (45), 86	87
C_{10} 	Ni[(–)-DIOP]$_2$ [c]	Alkene (7.4 mmol), cat (0.019 mmol), (–)-DIOP (0.12 mmol), hydroquinone (0.4 mmol), HCN (7.4 mmol), C_6H_6, 120°, 18 h	 (70), <5	63
	$Ni(cod)_2$ + **L2**	Alkene (0.5 mmol), $Ni(cod)_2$ (3 mol %), **L2** (2.1 mol %), HCN (0.48 mmol), toluene, 12–48 h	 Ligand **L2a** (75), 78 **L2c** (92), 72 **L2d** (87), 78	53
C_{11} 	$Ni(cod)_2$ + **L2a**	Alkene (0.5 mmol), $Ni(cod)_2$ (3 mol %), **L2a** (2.1 mol %), HCN (0.48 mmol), toluene, 12–48 h	 (56), 68[b]	53

TABLE 4A. ASYMMETRIC HYDROCYANATION OF MONOENES AND 1,3-DIENES (*Continued*)

Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_{11} 	$Ni(cod)_2$ + **L2**	Alkene (0.5 mmol), $Ni(cod)_2$ (3 mol %), **L2** (2.1 mol %), HCN (0.48 mmol), toluene, 12–48 h	 Ligand **L2a** (61), 68[b] **L2b** (46), 74[b] **L2c** (68), 66[b] **L2d** (62), 70[b]	53
	$Ni(cod)_2$ + **L2a**	Alkene (0.5 mmol), $Ni(cod)_2$ (3 mol %), **L2a** (2.1 mol %), HCN (0.48 mmol), toluene, 12–48 h	 (48), 19[b]	53
C_{12} 	$Ni(cod)_2$ + **L2**	Alkene (0.5 mmol), $Ni(cod)_2$ (3 mol %), **L2** (1 mol %), HCN (0.48 mmol), toluene, 12–48 h	 Ligand **L2a** (63), 75 **L2c** (64), 39 **L2d** (73), 50	53

[a] The selectivity refers to formation of the internal nitrile versus other products. No terminal nitrile was observed.
[b] The configuration of the product was not specified.
[c] The complex $Pd(DIOP)_2$ or $Ni(DIOP)_2$ and the corresponding ligand have opposite optical rotations.

TABLE 4B. ASYMMETRIC HYDROCYANATION OF BICYCLIC ALKENES

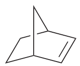
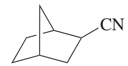
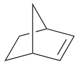
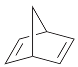
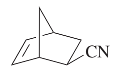
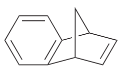
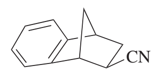
Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_7 	$Ni(cod)_2$ + **L1**	Alkene/$Ni(cod)_2$/**L1** (200:1:2), alkene/acetone cyanohydrin (>1:1), C_6H_6, 100°, 24 h	 (+)-**I** (52), 40	50
	$Pd_2(dba)_3$ + **L1**	Alkene (6 mmol), $Pd_2(dba)_3$ (0.03 mmol), **L1** (0.03 mmol), acetone cyanohydrin (5.5 mmol), C_6H_6 (0.5 mL), 120°, 18 h	(+)-**I** (52), 48	50
	Pd[(+)-DIOP]$_2$ [a]	Alkene (64 mmol), cat (0.09 mmol), (+)-DIOP (0.6 mmol), HCN (32 mmol), C_6H_6 (25 mL), 80°	(+)-**I** (94), 32	124, 47
	Pd[(+)-DIOP]$_2$ [a]	Alkene (28 mmol), cat (0.02 mmol), (+)-DIOP (0.2 mmol), HCN (14 mmol), C_6H_6 (7 mL), 120°, 18 h	(+)-**I** (94), 13	48
	Ni[(+)-DIOP)]$_2$ [a]	Alkene (64 mmol), cat (0.09 mmol), (+)-DIOP (0.6 mmol), HCN (32 mmol), C_6H_6 (25 mL), 80°	(–)-**I** (20), 14	124, 47
	Pd(**L16**)$_2$	Alkene (28 mmol), cat (0.02 mmol), **L16** (0.2 mmol), HCN (14 mmol), C_6H_6 (7 mL), 120°, 18 h	(–)-**I** (68), 20	48
	Pd[(*R*)-BINAP]$_2$	Alkene (28 mmol), cat (0.02 mmol), (*R*)-BINAP (0.2 mmol), HCN (14 mmol), C_6H_6 (7 mL), 120°, 18 h	(–)-**I** (6), 40	48

TABLE 4B. ASYMMETRIC HYDROCYANATION OF BICYCLIC ALKENES (*Continued*)

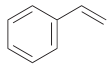
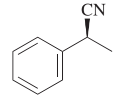
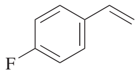
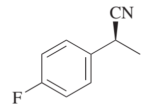
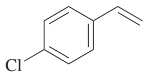
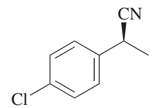
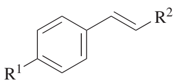
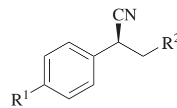
Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_7 	Ni(**L13**)$_2$	Alkene (48 mmol), cat (0.068 mmol), acetone cyanohydrin (24 mmol), 120°, 40 h	 (42), 33 (–)-**I**	49
	Ni(**L13**)$_2$	Alkene (48 mmol), cat (0.068 mmol), BPh_3 (0.34 mmol), acetone cyanohydrin (24 mmol), 100°, 40 h	(–)-**I** (58), 38	49
	Ni(cod)$_2$ + **L12**	Alkene/Ni(cod)$_2$/**L12**/acetone cyanohydrin (100:1:7:110), toluene, 100°, 24 h	**I**[b] 89% conv., 84% selectivity,[c] 55% ee	51
	Pd[(+)-DIOP]$_2$ [a]	Alkene (64 mmol), cat (0.09 mmol), (+)-DIOP (0.025 mmol), HCN (64 mmol), C_6H_6, 130°	 (40), 17	124, 47
C_{11} 	Pd[(+)-DIOP]$_2$ [a]	Alkene (37 mmol), cat (0.09 mmol), (+)-DIOP (0.6 mmol), HCN (32 mmol), C_6H_6 (25 mL), 130°, 18 h	 (83), 12	124, 47

[a] The complex Pd(DIOP)$_2$ or Ni(DIOP)$_2$ and the corresponding ligand have opposite optical rotations.

[b] The product configuration was not reported.

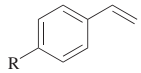
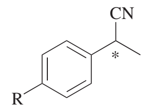
[c] The selectivity refers to formation of the nitrile versus other products.

TABLE 4C. ASYMMETRIC HYDROCYANATION OF VINYLARENES

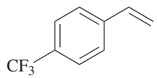
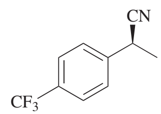
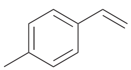
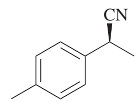
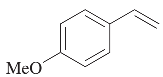
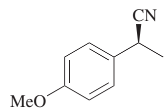
Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_8 	$Ni(cod)_2$ + **L17**	Alkene (1.3 mmol), $Ni(cod)_2$ (0.065 mmol), **L17** (0.062 mmol), HCN (1.04 mmol), toluene (2 mL), 60°, 16 h	 Ligand **L17a** (61), 12 **L17b** (81), 14 **L17c** (17), 42	127
	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >90% conv. Ligand — % ee **L2a** 28 **L2b** 15 **L2c** 4	45
	$Ni(cod)_2$ + **L2a**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2a** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >90% conv., 40% ee	45
C_{8-9} 	$Ni(cod)_2$ + **L4** or **L5**	Alkene/$Ni(cod)_2$/**L**/HCN (100:1:1.1:200), toluene (1.2 mL), 4 h		87

R^1	R^2	Ligand	Temp (°)	Product Yield (%), % ee
H	H	**L4**	60	(100), 43
H	H	**L4**	0	(69), 47
H	H	**L5**	60	(100), 34
H	H	**L5**	0	(100), 49
Me	H	**L4**	0	(100), 54
Me	H	**L5**	0	(100), 50
H	Me	**L5**	60	(24), 30

TABLE 4C. ASYMMETRIC HYDROCYANATION OF VINYLARENES (*Continued*)

Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_{8-12} 	$Ni(cod)_2$ + **L12**	Alkene/$Ni(cod)_2$/**L12**/acetone cyanohydrin (100:1:x:110), toluene, 100°, 24 h		51

R	x	Conv. (%)	Selectivity (%)[a]	% ee[b]
H	1.2	48	70	49
F	7	98	94	49
Me	7	98	80	41
MeO	7	98	83	40

Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_9 	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >90% conv.	45
	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >90% conv.	45
	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >90% conv.	45

CF_3 substrate:

Ligand	% ee
L2a	14
L2b	9
L2c	<5

Methyl substrate:

Ligand	% ee
L2a	70
L2b	47
L2c	<5

MeO substrate:

Ligand	% ee
L2a	52
L2b	39
L2c	6

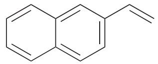
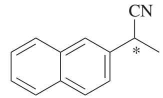
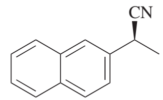
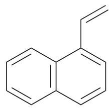
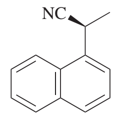
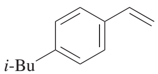
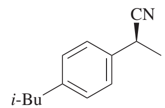
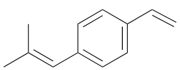
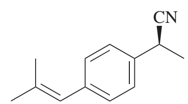
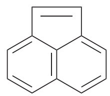
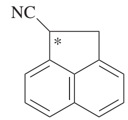
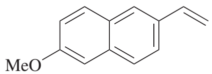
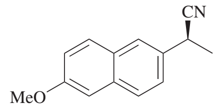
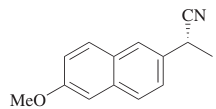
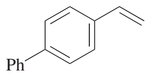
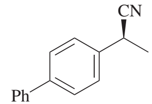
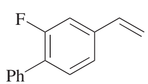
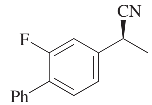
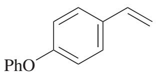
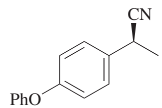
C_{12} 	$Ni(cod)_2$ + **L12**	Alkene/$Ni(cod)_2$/**L12**/acetone cyanohydrin (100:1:7:110), toluene, 100°, 24 h	 20% conv., 94% selectivity,[a] 38% ee[b]	51
	$Ni(cod)_2$ + **L2**	Alkene (22 mmol), $Ni(cod)_2$ (1 mol %), **L2** (1 mol %), HCN (22 mmol), toluene, 24 h	 >95% conv. Ligand — % ee **L2a** 77 **L2b** 75 **L2c** 46 **L2d** 25	45
	$Ni(cod)_2$ + **L2**	Alkene (22 mmol), $Ni(cod)_2$ (1 mol %), **L2** (1 mol %), HCN (22 mmol), toluene, 24 h	 >95% conv. Ligand — % ee **L2a** 68 **L2c** 63	45
	$Ni(cod)_2$ + **L17**	Alkene/$Ni(cod)_2$/**L17**/HCN (100:1:1.05:125), toluene (2 mL), 60°, 16 h	 **I** Ligand **L17a** (29), 19 **L17b** (58), 15 **L17c** (22), 63	127
	$Ni(cod)_2$ + **L2**	Alkene (7.92 mmol), $Ni(cod)_2$ (0.16 mol %), **L2** (0.16 mol %), HCN (11 mmol in toluene), hexane, 24 h	**I** Ligand **L2a** (77), 56 **L2b** (—), 38 **L2c** (—), 6	45
	$Ni(cod)_2$ + **L2a**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2a** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 (—), 63	45

TABLE 4C. ASYMMETRIC HYDROCYANATION OF VINYLARENES (*Continued*)

Alkene	Catalyst	Conditions	Product(s) and Yield(s) (%), % ee	Refs.
C_{12} 	$Ni(cod)_2$ + **L2**	Alkene (22 mmol), $Ni(cod)_2$ (1 mol %), **L2** (1 mol %), HCN (22 mmol), toluene, 24 h	 >95% conv. Ligand — % ee[b] **L2a** — 59 **L2c** — 0	45
C_{13} 	$Ni(cod)_2$ + **L17**	Alkene/$Ni(cod)_2$/**L17**/HCN (20:1:1.05:205), toluene (2 mL), 60°, 16 h	 **I** Ligand **L17a** — (99), 31 **L17b** — (99), 30 **L17c** — (99), 29	127
	$Ni(cod)_2$ + **L2**	Alkene (22 mmol), $Ni(cod)_2$ (1 mol %), **L2** (1 mol %), HCN (22 mmol), toluene, 24 h	**I** >95% conv. Ligand — % ee **L2a** — 84[c] **L2b** — 78 **L2c** — 35 **L2d** — 16	45
	$Ni(cod)_2$ + **L14**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L14** (2 mol %), HCN (0.65 mmol), 24 h	 **II** >95% conv. Ligand — % ee **L14a** — 33 **L14c** — 13	89
	$Ni(cod)_2$ + **L3**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L3** (2 mol %), HCN (0.65 mmol), rt, 24 h	**II** >95% conv. Ligand — % ee **L3a** — 56 **L3b** — 43 **L3c** — 58 **L3d** — 89[d]	86

	$Ni(cod)_2$ + **L15**	Alkene, $Ni(cod)_2$ (2 mol %), **L15** (2 mol %), HCN, 24 h	**II** (—) Ligand % ee **L15a** 70 **L15b** 54 **L15c** 77	86
C_{14} 	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 >95% conv. Ligand % ee **L2a** 68 **L2b** 41 **L2c** 8	45
	$Ni(cod)_2$ + **L2**	Alkene (22 mmol), $Ni(cod)_2$ (1 mol %), **L2** (1 mol %), HCN (22 mmol), toluene, 24 h	 90% conv. Ligand % ee **L2a** 55 **L2c** 10	45
	$Ni(cod)_2$ + **L2**	Alkene (0.65 mmol), $Ni(cod)_2$ (2 mol %), **L2** (2 mol %), HCN (0.65 mmol), hexane, 24 h	 90% conv. Ligand % ee **L2a** 60 **L2b** 38 **L2c** 7	45

[a] The selectivity refers to formation of the branched nitrile versus other products. No linear nitrile was observed.

[b] The absolute configuration of the product was not reported.

[c] Recrystallization of the product increases the enantiomeric excess from 84 to 99% ee.

[d] The enantiomeric excess increases from 89 to 95% ee when the reaction is performed at 0º.

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CHAPTER 2

INTERMOLECULAR C–H INSERTIONS OF CARBENOIDS

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INTRODUCTION

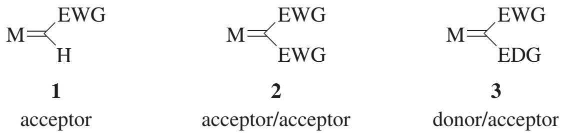
The metal-catalyzed reactions of diazo compounds have broad utility in organic synthesis. The resulting high-energy metal carbenoid intermediates are capable

of a range of useful transformations, including cyclopropanation, ylide formation, and C–H insertion. Three *Organic Reactions* chapters have been published on different aspects of the reactions of diazo compounds. A chapter in 1970 described the intermolecular reactions of ethyl diazoacetate with alkenes and aromatic systems.[1] This was followed by a review in 1979 on intramolecular reactions of metal carbenoids.[2] The pace of research in this area has greatly increased in recent years, especially since the development of a range of chiral catalysts,[3,4] rendering the transformations highly chemoselective and enantioselective. Several excellent reviews[5–31] and an authoritative book[32] have appeared on various aspects of intramolecular reactions of metal carbenoids. Intermolecular cyclopropanations were covered in a 2001 *Organic Reactions* chapter.[33] This chapter provides a comprehensive overview of intermolecular C–H insertion, a process that has rapidly developed over the last decade. The literature is covered through June 2008.

The intermolecular C–H insertion by metal carbenoids is arguably the most versatile reaction to date for stereoselective C–H functionalization.[34,35] A synthetically useful reaction would require C–H insertion to be site selective. To attain this, most of the early work was conducted using intramolecular versions of this reaction in which the site of functionalization could be readily controlled.[36] In the last decade, however, considerable progress has been made in developing highly efficient intermolecular C–H insertions.[34,37–42] This review covers the historical background of intermolecular C–H insertions and describes how the utilization of new catalysts and more stabilized carbenoids has resulted in major advances in this field. Now that highly diastereoselective and enantioselective C–H functionalization can be achieved, the method can be effectively applied to the synthesis of pharmaceutical agents and natural products.[34]

This review will focus exclusively on intermolecular C–H insertions of metal carbenoids into sp^3-hybridized C–H bonds. Although a number of functionalizations of aromatic and vinylic C–H bonds are known,[32] they will not be covered here because these reactions are more representative of electrophilic substitution. In other words, they most likely proceed by electrophilic addition of the carbenoid to a π-system followed by proton loss, and do not involve a direct C–H insertion. The intramolecular C–H insertion of metal carbenoids has been extensively reviewed and is outside the scope of this review.[4,32,36,43,44]

Before the mechanism of carbenoid C–H insertions can be discussed, it is necessary to consider the three major classes of carbenoid intermediates that are involved in these reactions. Metal carbenoids are highly electrophilic reagents. Their reactivity can be influenced by many factors including the nature of the metal and the ligands associated with it, but the most dramatic influence is exerted by the carbenoid structure. The carbenoids can be classified into three major classes: (1) acceptor-substituted carbenoids, (2) acceptor/acceptor-substituted carbenoids, and (3) donor/acceptor-substituted carbenoids (Fig. 1, note that "acceptor-substituted carbenoids" will subsequently be referred to as "acceptor carbenoids").[33] The acceptor carbenoids have only a single electron-withdrawing group; the prototypical example is the carbenoid derived from ethyl diazoacetate.



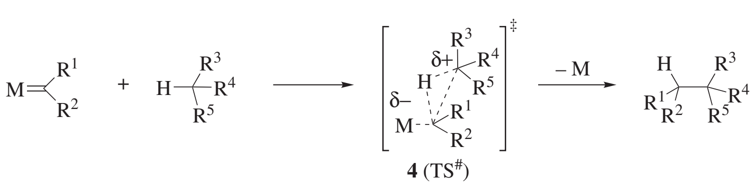
EWG = CO_2R, COR, NO_2, $PO(OR)_2$, CF_3 or SO_2R
EDG = vinyl, aryl, or heteroaryl

Figure 1. Major classes of metal carbenoids.

The acceptor/acceptor carbenoids are substituted by two electron-withdrawing groups; the most common examples are the carbenoids derived from dimethyl diazomalonate and methyl diazoacetoacetate. The presence of only electron-withdrawing groups makes the carbenoids highly reactive but less selective, particularly in intermolecular reactions. The donor/acceptor carbenoids, in which the donor group modulates the electrophilic character of the carbenoid, are more selective intermediates than the other classes of carbenoids.[45] Typical donor groups are substituted vinyl and aryl groups, which are capable of stabilizing the electron-deficient carbenoid site by means of π-donation.

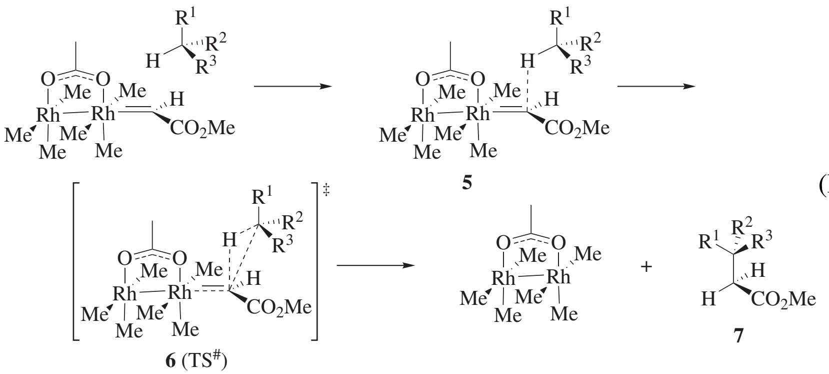
MECHANISM AND STEREOCHEMISTRY

During the early stages of development of the carbenoid C–H insertion methodology, the mechanistic details were not well understood. The mechanistic hypotheses about the reactions of the carbenoids were made on the basis of the site- and stereoselectivity of C–H insertions.[46–48] The mechanism that gained the most support was one that involves a concerted but non-synchronous C–H insertion in which build-up of positive charge occurred on the sp^3 carbon as illustrated with transition structure **4** (Eq. 1).[32] Evidence to support this mechanism comes from observations that the insertion occurs with retention of configuration at the sp^3 carbon, and that electron-donating groups activate this site, whereas electron-withdrawing groups deactivate the site toward C–H insertion. Hammett studies confirmed that the reaction proceeds with build-up of positive charge at the sp^3 carbon[49–51] and deuterium kinetic isotope effect studies[52,53] showed that cleavage of the C–H bond is involved in the rate-determining step. The metal carbenoid intermediate is considered to be very reactive, and this is also consistent with the Hammett and Kinetic Isotope Effect (KIE) studies. The relatively small values observed for ρ and KIE, respectively, indicate that the C–H insertion proceeds through a very early transition structure.[49–53]



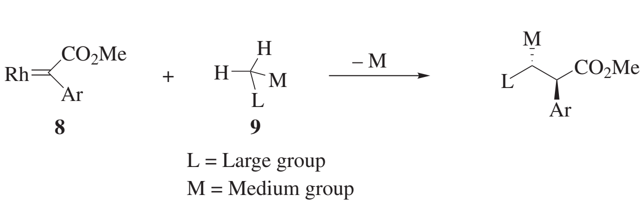
(Eq. 1)

Theoretical studies on the mechanism of the rhodium-catalyzed C–H insertions of ethyl diazoacetate to alkanes have added considerable insight.[54,55] These studies suggest that the reaction proceeds in a concerted non-synchronous manner with the reaction initiating as a hydride transfer event (**5**) (Eq. 2). Before the hydride transfer is complete, however, the carbon–carbon bond-forming event (**6**) occurs, such that the insertion product **7** is formed with overall retention of configuration at the sp^3 carbon. The activation energy for the C–H insertion step is very small (~0.2 kcal/mol for a secondary C–H bond), and normally quite exothermic (~50 kcal/mol), which is consistent with this step proceeding through an early transition state structure.



(Eq. 2)

The donor/acceptor carbenoids have an entirely different reactivity/selectivity profile than the acceptor carbenoids.[33] Because of the added stability imparted by the donor group, these carbenoids are capable of highly selective intermolecular C–H insertions. The C–H insertion by aryldiazoacetate-derived carbenoid **8** into compounds bearing secondary C–H sites with substituents of different sizes (**9**) occurs in many instances with high diastereoselectivity (>19:1 dr), as illustrated in Eq. 3.[33]



(Eq. 3)

A model has been developed to explain the diastereoselectivity of this C–H insertion (Fig. 2).[37,40,53,56] The reaction is initiated by a hydride transfer in an analogous manner to the Nakamura model,[54,55] but the orientation of the substrate is more ordered than it is in the case of the reactions of ethyl diazoacetate. The substrate approaches in an orientation such that the large group (L) points away from the rhodium atom, while the second largest group points toward the aryl group. Calculations have shown that the alkoxy moiety of the ester group on the carbenoid lies orthogonal to the rhodium carbenoid plane and sterically

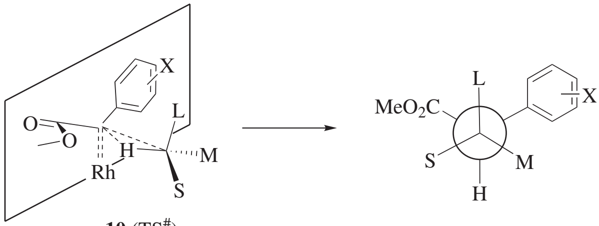
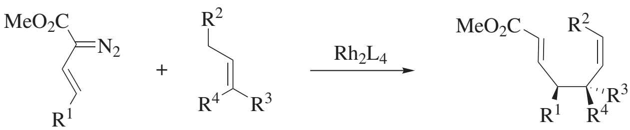


Figure 2. Model for C–H insertion by aryldiazoacetates.

interferes with the approach of the substrate.[56] Consequently, the smallest group (S) on the substrate is oriented toward the ester group of the carbenoid. Specific examples of these highly diastereoselective reactions are described in the Scope and Limitations section.

The site selectivity in the C–H insertion by donor/acceptor carbenoids is controlled by a delicate balance of steric and electronic effects. The carbenoid carbon preferentially attacks C–H bonds where the tetrahedral carbon in transition structure **10** can stabilize positive charge build-up. This is counterbalanced by steric effects, because the carbenoid acts as a sterically demanding agent. Consequently, an electronically activated but sterically crowded C–H bond can be totally unreactive toward donor/acceptor carbenoids.[37,40,41]

The reaction of vinyldiazoacetates with compounds containing allylic C–H bonds results in an unusual reaction, called the "combined C–H activation/Cope rearrangement" (Eq. 4).[41,57] It is highly stereoselective, generally producing only a single diastereomer and double bond isomer of product **11**.[57] The direct C–H insertion product is not an intermediate in this reaction, because such a product is generally thermodynamically more stable than the observed one.



(Eq. 4)

The mechanism of this reaction has not yet been determined, but it has been proposed to begin with an abortive C–H insertion event (Fig. 3). Before that process is complete, however, a reaction analogous to a Cope rearrangement occurs, as illustrated in transition structure **12**, to generate the rearranged product. Because of the chair-like transition structure of the Cope rearrangement in **12**, the reaction is highly diastereoselective.[57] The R^2 substituent in **12** adopts an axial position, presumably to avoid interaction with the surface of the catalyst, generating a *cis*-alkene in the product. As illustrated in Fig. 2, large groups on the substrate will tend to point away from the catalyst surface to avoid steric interactions.

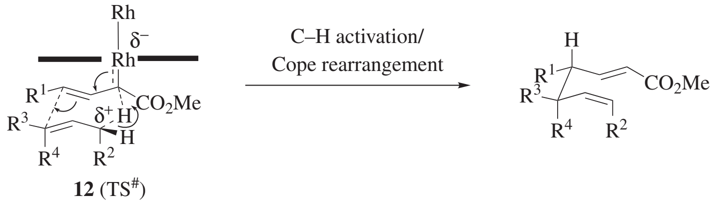


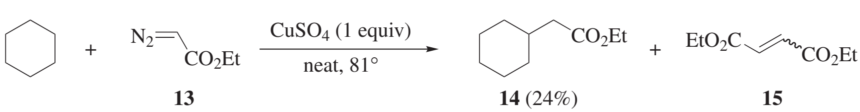
Figure 3. Transition structure model for the combined C–H activation/Cope rearrangement.

SCOPE AND LIMITATIONS

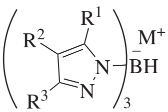
Intermolecular C–H insertions have been primarily conducted with four types of carbenoid intermediates: the acceptor carbenoids, the acceptor/acceptor carbenoids, and two types of donor/acceptor carbenoids (derived from either aryldiazoacetates or vinyldiazoacetates). Because the four systems have distinct influences on the outcome of the C–H functionalization process, their scope and limitations will be described separately. The early studies on intermolecular C–H insertions used primarily ethyl diazoacetate as the carbenoid source.[58–62] Because the carbenoid from ethyl diazoacetate is an acceptor carbenoid, it is highly reactive, relatively unselective, and prone to dimerization, limiting its effectiveness in C–H insertions.[63,64] A limited number of C–H insertions with acceptor/acceptor carbenoids are known but this area is not well developed.[65] In contrast, various aryldiazoacetate derivatives have been used in a wide number of highly site-, diastereo- and enantioselective reactions.[40] Donor/acceptor carbenoids derived from vinyldiazoacetates are considered as a separate class because they have been extensively applied to the combined C–H activation/Cope rearrangement.[41]

Acceptor Carbenoids

Reaction with Hydrocarbons. The first authentic example of a metal-catalyzed intermolecular C–H insertion, which was described in 1974, is the copper(II) sulfate-catalyzed reaction of ethyl diazoacetate (**13**) in cyclohexane as solvent (Eq. 5).[58] C–H insertion product **14** was formed in 24% yield. Even though the ethyl diazoacetate was added slowly to achieve simulated high dilution conditions, the major products were diethyl fumarate and diethyl maleate (**15**). In the early 1980's, higher-yielding procedures for the C–H functionalization of hydrocarbons were developed using dirhodium tetrakis(trifluoroacetate)[61,62] and rhodium porphyrin complexes.[59,60] The reaction was applied to the functionalization of linear and branched alkanes, but these reactions gave mixtures of C–H insertion products.



(Eq. 5)



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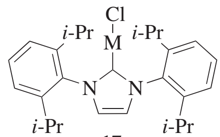


17

+ $NaBAr_4$

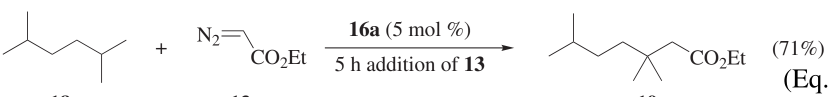
Ar = 3,5-$(CF_3)_2C_6H_3$

	M	R^1	R^2	R^3	
16a:	Cu	Br	Br	Br	Tp^{Br3}
16b:	Cu	H	H	Mes	Tp^{Ms}
16c:	Cu	Cy	H	H	Tp^{Cy}
16d:	Ag	CF_3	H	CF_3	

	M
17a:	Cu
17b:	Au

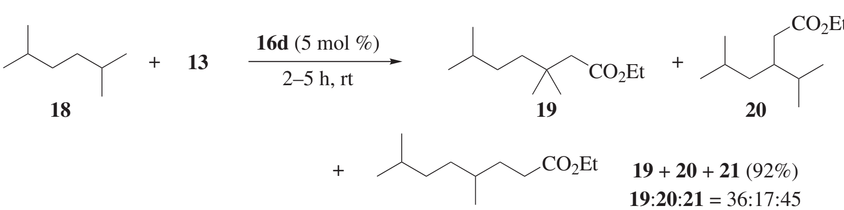
Figure 4. Copper and silver catalysts with sterically hindered ligands.

In recent years the scope of intermolecular C–H insertions has been improved with the development of copper and silver catalysts containing bulky ligands.[63,64] A variety of bulky tridentate scorpionate complexes **16**[66–73] have been used as well as the heterocyclic nucleophilic carbene complexes **17**[133] (Fig. 4). Because of the bulky nature of these catalysts, the carbenoid is less prone to undergo the undesired carbene dimerization. A mixture of products derived from C–H functionalization at both secondary and tertiary C–H bonds is common, but by judicious choice of hydrocarbon substrates, selective functionalization can be achieved as illustrated in Eq. 6.[68] The secondary C–H bonds in 2,5-dimethylhexane (**18**) are sterically crowded compared to a methylene group in a linear hydrocarbon; therefore, the C–H insertion occurs exclusively at the tertiary site, which is electronically more favored than the primary site, to form ester **19** in 71% yield. In general, the copper-catalyzed reactions tend to occur preferentially at tertiary and secondary C–H sites over primary C–H sites while the silver-catalyzed reactions have an enhanced tendency toward insertion at a primary C–H bond, although mixtures of products are typically formed.[63,64,66–73] A good illustration of these trends is the silver-catalyzed reaction of ethyl diazoacetate with 2,5-dimethylhexane (**18**), which generates a mixture of all three possible C–H insertion products **19–21** (Eq. 7).[71]



18 13 19

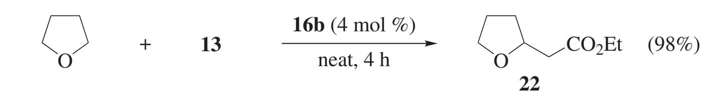
(Eq. 6)



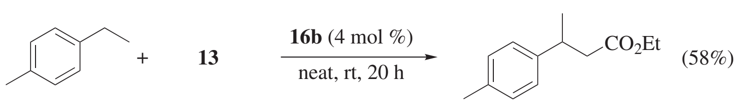
18 19 20 21

(Eq. 7)

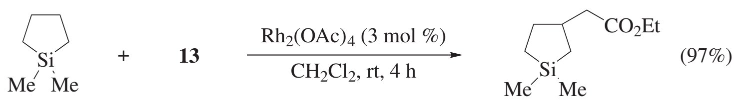
Reaction with Activated C–H Bonds. A substrate is activated toward C–H insertion when it contains functionality that can support the partial charge build-up that is associated with the C–H insertion event. In particular, C–H bonds that are allylic, benzylic, α to an oxygen- or nitrogen-containing functionality, or β to silicon are especially favorable for C–H insertion. Representative examples are illustrated in Eqs. 8–10. The bulky copper catalyst **16b** promotes the reaction of ethyl diazoacetate with neat tetrahydrofuran to generate C–H insertion product **22** in 98% yield.[66,67] Catalyst **16b** also promotes the selective insertion of ethyl diazoacetate at the secondary C–H bond of 4-ethyltoluene (**23**) to form product **24** in 58% yield.[70] A remarkably efficient C–H insertion is the rhodium acetate catalyzed reaction of ethyl diazoacetate with silacyclopentane **25**, which results in the formation of ester **26** in 97% yield.[74] A single stereogenic center is generated in these C–H insertions of acceptor carbenoids and no diastereoselective C–H insertions into chiral substrates have been reported. No successful enantioselective intermolecular C–H insertions with acceptor carbenoids have been reported to date.



(Eq. 8)



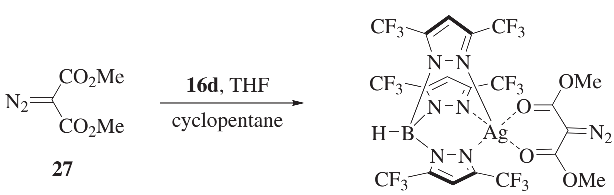
23 **24** (Eq. 9)



25 **26** (Eq. 10)

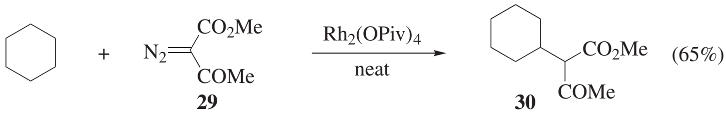
Acceptor/Acceptor Carbenoids

Intermolecular C–H insertions with acceptor/acceptor carbenoids have not been extensively studied. The new bulky catalysts such as **16** are not effective at promoting nitrogen extrusion from dimethyl diazomalonate (**27**). Instead, silver complex **16d** reacts with dimethyl diazomalonate to form the stable complex **28** (Eq. 11).[64]



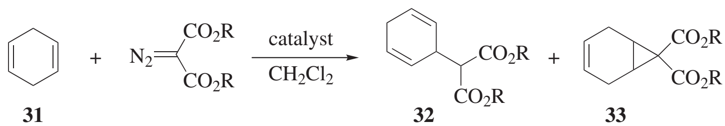
28 (Eq. 11)

Reaction with Hydrocarbons. Dirhodium tetracarboxylates are effective catalysts for the reaction of acceptor/acceptor carbenoids with hydrocarbons. Rhodium pivalate catalyzed reaction of methyl diazoacetoacetate (**29**) with cyclohexane generates the C–H insertion product **30** in 65% yield (Eq. 12).[75]



(Eq. 12)

Reaction with Activated C–H Bonds. Acceptor/acceptor carbenoids are capable of insertion into activated C–H bonds, but competing reactions are often dominant. The rhodium acetate catalyzed reaction of dimethyl diazomalonate with 1,4-cyclohexadiene (**31**) generates a 2:1 mixture of C–H insertion product **32** (R = Me) and cyclopropane **33** in 63% combined yield (Eq. 13).[76] Under copper catalysis, C–H insertion is less favored. When cuprous chloride is used as the catalyst with diethyl diazomalonate, only traces of C–H insertion product **32** (R = Et) are obtained (Eq. 13).[76]

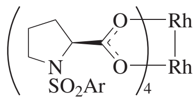


(Eq. 13)

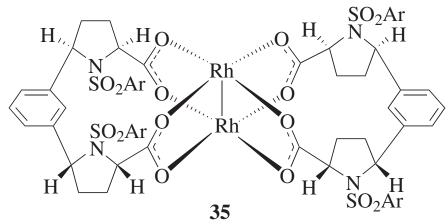
Catalyst	R	**32**	**33**
$Rh_2(OAc)_4$	Me	(42%)	(21%)
CuCl	Et	(2%)	(26%)

Donor/Acceptor Carbenoids Derived from Aryl- and Heteroaryldiazoacetates

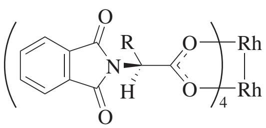
Intermolecular C–H insertions with aryldiazoacetates were first reported in 1997.[77] Since then, this reaction has been extensively developed because these carbenoids are capable of highly site-selective reactions with a range of substrates.[37,39–41] Insertions into secondary C–H bonds can be achieved with a high level of diastereoselectivity. Furthermore, chiral catalysts have been developed that are capable of high levels of asymmetric induction in these transformations; some of the most selective catalysts are shown in Fig. 5. The most extensively employed catalyst is the dirhodium tetraprolinate $Rh_2(S\text{-DOSP})_4$ (**34**).[49,53,57,77–110] This complex has been used with a wide variety of substrates and generally gives high enantioselectivity as long as the acceptor group of the donor/acceptor carbenoid is a methyl ester. A rigid variant is $Rh_2(S\text{-biDOSP})_2$ (**35**).[92] When catalyst **34** fails to give high asymmetric induction, the dirhodium tetracarboxylates $Rh_2(S\text{-PTAD})_4$ (**36**)[111] and $Rh_2(S\text{-PTTL})_4$ (**37**)[112] are effective complementary catalysts. The chiral copper catalyst Cu(BOX1) (**38**) can give moderate asymmetric induction, but lower levels than obtained with catalyst **34**.[113] The dirhodium tetracarboxamidate catalyst $Rh_2(S,R\text{-MenthAZ})_4$ (**39**) gave high asymmetric induction in an isolated case.[114]



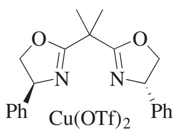
34
Ar = 4-$C_{12}H_{25}C_6H_4$
Rh_2(*S*-DOSP)$_4$



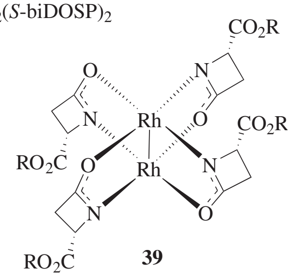
35
Ar = 4-$C_{12}H_{25}C_6H_4$
Rh_2(*S*-biDOSP)$_2$



	R	
36	Ad	Rh_2(*S*-PTAD)$_4$
37	*t*-Bu	Rh_2(*S*-PTTL)$_4$



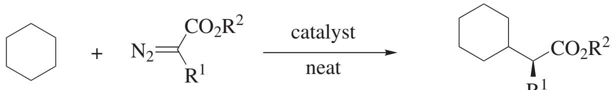
38
Cu(BOX1)



39
R = D-menthyl
Rh_2(*S*,*R*-MenthAZ)$_4$

Figure 5. Chiral catalysts for intermolecular C–H insertion.

Reaction with Hydrocarbons. The difference in reactivity between ethyl diazoacetate and aryldiazoacetates is readily seen in the rhodium-catalyzed reactions with cyclohexane under reflux conditions (Eq. 14). The rhodium pivalate catalyzed reaction of ethyl diazoacetate (**13**) generates C–H insertion product **14** in only 10% yield.[75] Dimerization of the carbene is the major reaction pathway. Under identical conditions, the reaction of methyl phenyldiazoacetate (**40**) gives a 94% yield of C–H insertion product **41**.[75] When the reaction is catalyzed by the chiral rhodium prolinate complex Rh_2(*S*-DOSP)$_4$ (**34**), **41** is formed in 83% yield and 81% ee.[77] When the same reaction is conducted at 10°, **41** is formed in 95% ee and comparable yield.[53]



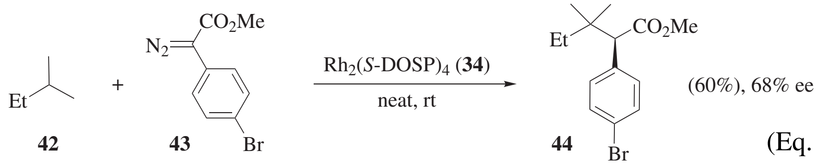
13 or **40**

(Eq. 14)

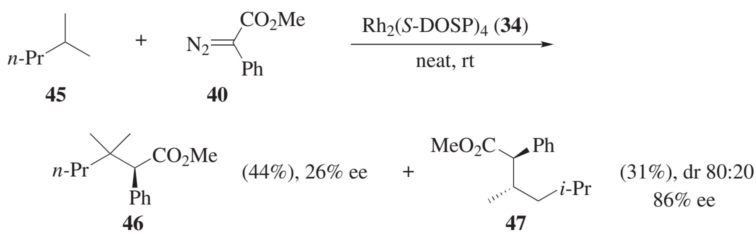
Carbenoid	R^1	R^2	Catalyst	Temp (°)	Product		% ee
13	H	Et	$Rh_2(OPiv)_4$	81	**14**	(10%)	—
40	Ph	Me	$Rh_2(OPiv)_4$	81	**41**	(94%)	—
40	Ph	Me	Rh_2(*S*-DOSP)$_4$ (**34**)	81	**41**	(83%)	81
40	Ph	Me	Rh_2(*S*-DOSP)$_4$ (**34**)	10	**41**	(80%)	95

Insertions into C–H bonds of acyclic alkanes illustrate some of the site selectivity associated with this reaction. The Rh_2(*S*-DOSP)$_4$ (**34**) catalyzed reaction of aryldiazoacetate **43** with 2-methylbutane (**42**) generates a single C–H insertion

product (**44**) in 60% yield (68% ee) (Eq. 15).[53] Only the tertiary C–H bond is functionalized. In contrast, the Rh_2(*S*-DOSP)$_4$ (**34**) catalyzed reaction of methyl phenyldiazoacetate (**40**) with 2-methylpentane (**45**) gives rise to two products, **46** and **47**, in 44% and 31% yield, respectively (Eq. 16).[53] These results indicate that sterically unencumbered secondary C–H bonds have similar reactivity to tertiary C–H bonds, while the sterically more crowded secondary C–H bonds (C-3) in **42** and **45** are significantly less reactive toward this carbenoid complex. Because hydrocarbons are, in general, less reactive than substrates that are activated for C–H insertion, certain hydrocarbons (e.g. hexane, pentane) can be used as inert solvents for the reactive substrates. In reactions with less reactive systems, a commonly used inert solvent is 2,2-dimethylbutane (DMB), which contains only primary and sterically crowded secondary C–H bonds.



(Eq. 15)

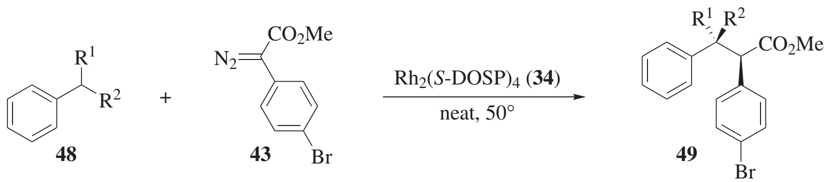


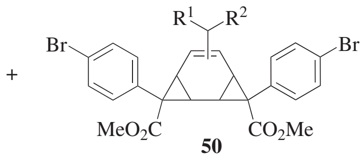
(Eq. 16)

Reaction with Activated C–H Bonds. The carbenoid insertion into activated C–H bonds has broad synthetic utility. The types of C–H bonds that have been most extensively functionalized are those at benzylic[49,91,112] and allylic positions,[41,57,76,79,81–85,87,89,90,95,97–100,103,104,109] as well as sites α to oxygen[53,79,82,90,94,112] and nitrogen functionalities.[80,92,96,98,105,115] This section will begin by discussing the site selectivity and stereoselectivity associated with this process, followed by a description of the most illustrative examples of insertions at specific types of activated C–H bonds.

Site Selectivity, Diastereoselectivity, and Enantioselectivity. The site selectivity of the C–H insertion is controlled by a balance of steric and electronic effects. As the C–H insertion is initiated by a hydride abstraction, sites that effectively stabilize positive charge build-up at the sp^3 carbon center are more reactive, but this electronic effect can be offset by the steric demands of the carbenoid complex. A tertiary C–H bond is the most electronically activated but it is also the most sterically crowded. Consequently, in many instances a secondary C–H bond is the favored site for insertion because it has the best balance of electronic activation and steric accessibility. A good example of this trend is the

reaction with toluene, ethylbenzene, and cumene (Eq. 17).[49] The $Rh_2(S\text{-DOSP})_4$ (**34**) catalyzed reactions of aryldiazoacetate **43** with toluene (**48a**) and cumene (**48c**) give large amounts of double cyclopropanation products **50**. However, only a trace amount of **50** forms in the reaction with ethylbenzene (**48b**) and C–H insertion product **49b** is isolated in 49% yield, 84:16 dr, and 86% ee.

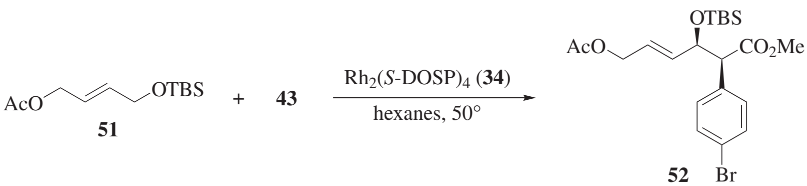




Product	R^1	R^2	**49:50**
49a, **50a**	H	H	28:72
49b, **50b**	Me	H	>90:10
49c, **50c**	Me	Me	60:40

(Eq. 17)

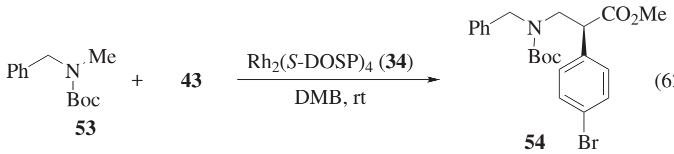
Selective C–H insertion into one of two sterically equivalent C–H bonds can be achieved by influencing the electron density at the two sites. A clear example of this effect is the reaction of aryl diazoacetate **43** with the differentially protected diol **51** (Eq. 18).[90] The acetoxy group is electron withdrawing, causing the C–H insertion to occur exclusively at the methylene group α to the silyloxy group to form ester **52**. This example is also a good illustration of the diastereocontrol that is possible. High diastereoselectivity can be achieved when the C–H insertion occurs at methylene sites with good size differentiation between the other two groups. Furthermore, $Rh_2(S\text{-DOSP})_4$ (**34**) is routinely used in these reactions because if the acceptor group in the donor/acceptor carbenoid is a methyl ester, then this catalyst furnishes products with high enantioselectivity (70–95% ee) in most instances. A further advantage of catalyst **34** is its tendency to give higher yields of C–H insertion products than most other catalysts.[53]



(Eq. 18)

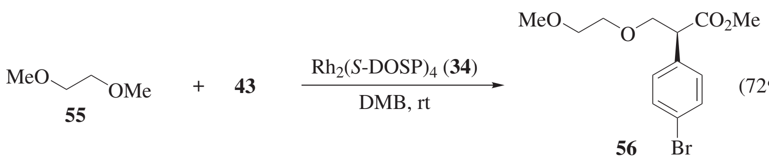
(93%), dr >97:3, 62% ee

Steric crowding can override electronic factors in determining selectivity, as shown in the reaction with *N*-Boc-protected *N*-methyl-*N*-benzylamine (**53**).[88] Even though the benzylic group is an excellent site for stabilizing positive charge build-up, the reaction occurs exclusively at the primary C–H bond to form ester **54** with 95% ee (Eq. 19).



(62%), 95% ee (Eq. 19)

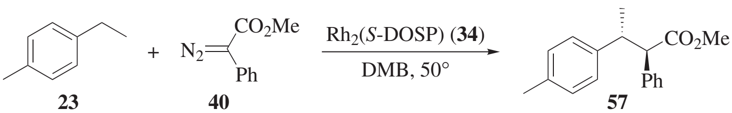
Even though an α-oxygen substituent activates a geminal C−H bond toward insertion, a β-oxygen substituent is deactivating because of an inductive effect. A simple substrate that illustrates this effect is 1,2-dimethoxyethane (**55**) (Eq. 20).[94] The Rh_2(*S*-DOSP)$_4$ (**34**) catalyzed reaction of aryldiazoacetate **43** with 1,2-dimethoxyethane (**55**) generates a single C−H insertion product **56**, selectively functionalizing the primary C−H bond over the secondary C−H bond. This results from deactivation of the methylene sites by the presence of the β-oxygen functionality.



(72%), 76% ee

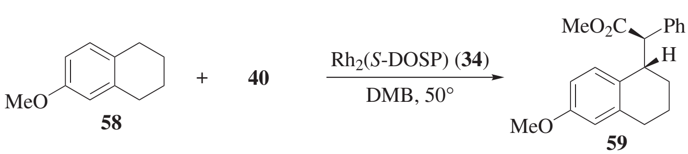
(Eq. 20)

C−H Insertion at Benzylic Sites. Monosubstituted benzene derivatives are not ideal substrates for C−H insertions because they are prone to double cyclopropanation of the aromatic ring. If the ring is 1,4-disubstituted, it is sterically protected from cyclopropanation reaction with donor/acceptor carbenoids. Thus, 4-ethyltoluene (**23**) undergoes a clean C−H insertion at the benzylic methylene site with phenyldiazoacetate **40** to form ester **57** in 64% yield (Eq. 21).[49] No insertion occurs at the benzylic methyl site. A Hammett study of 4-substituted ethylbenzene derivatives showed that a positive charge build-up occurs on the sp^3 carbon in the transition structure which is stabilized by resonance.[49] A synthetic example that illustrates this behavior is the reaction with tetrahydronaphthalene **58** (Eq. 22).[49] The major C−H insertion product **59** is produced with a 98:2 site selectivity and is derived from reaction at the benzylic site *para* to the methoxy group.



(64%), dr 82:28
89% ee

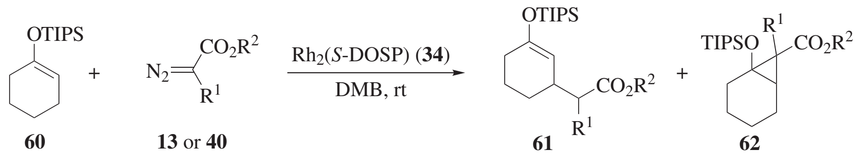
(Eq. 21)



(77%), dr 80:20
94% ee

(Eq. 22)

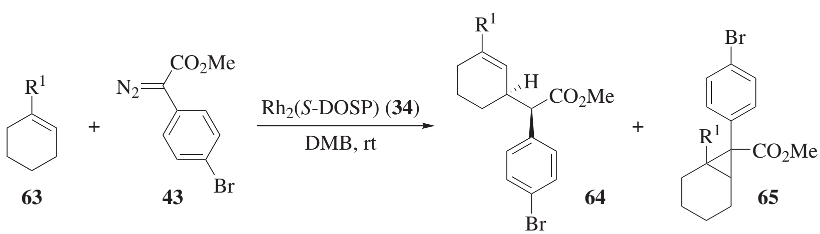
C–H Insertion at Allylic Sites. Insertion at allylic C–H sites is complicated by the possibility of competing cyclopropanation. Because of the steric demands of donor/acceptor carbenoids, they tend to efficiently cyclopropanate 1-substituted and 1,1-disubstituted alkenes, whereas 1,2-*cis*-disubstituted alkenes are less effective as substrates for cyclopropanation.[33] 1,2-*trans*-Disubstituted alkenes and more highly functionalized alkenes do not undergo cyclopropanation unless they are very electron rich.[109] An illustration of this concept is seen in the reaction with siloxycyclohexene **60** (Eq. 23).[84] The $Rh_2(S\text{-DOSP})_4$ (**34**) catalyzed reaction of aryldiazoacetate **40** with siloxycyclohexene **60** generates the C–H insertion product **61a** cleanly as a mixture of diastereomers without any cyclopropanation of the electron-rich double bond. In contrast, the reaction with ethyl diazoacetate (**13**) affords predominantly cyclopropane **62b**.



(Eq. 23)

Carbenoid	R^1	R^2	Product	**61** + **62**	**61**:**62**
40	Ph	Me	**61a**, **62a**	**61a** (90%)	—
13	H	Et	**61b**, **62b**	(54%)	24:76

The reaction of aryl diazoacetate **43** with cyclohexene (**63a**) leads to both C–H insertion product **64a** and cyclopropane **65a** (Eq. 24).[76,85] Furthermore, **64a** is formed as a 55:45 mixture of diastereomers. The cyclopropanation can be blocked by introduction of sterically demanding substituents on the alkene. Thus, alkenylsilane **63b** selectively affords C–H insertion product **64b**.[85] Furthermore, because of the size difference between the two groups on the alkenes, the diastereoselectivity is improved to 94:6. Once again, $Rh_2(S\text{-DOSP})_4$ (**34**) is a very effective chiral catalyst and **64b** is produced with 95% ee.

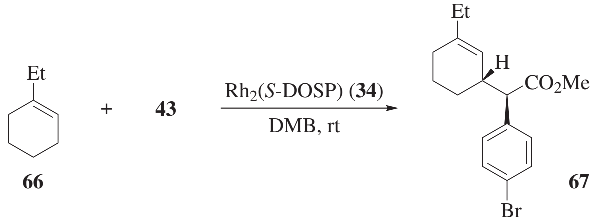


(Eq. 24)

Product	R^1	**64**	dr **64**	% ee **64**	**65**
64a, **65a**	H	(58%)	55:45	93	(15)
64b, **65b**	TBDPS	(64%)	94:6	95	(0)

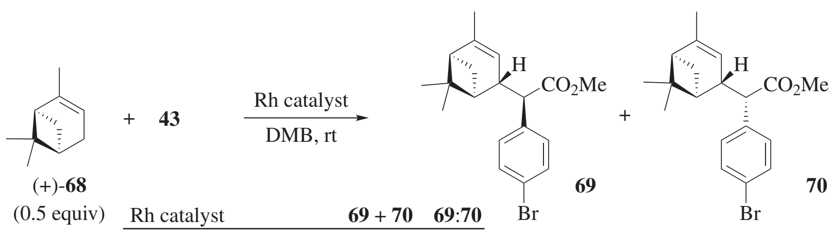
The steric influences on the substrate reactivity can result in a highly site-selective C–H insertion. One such example is the reaction with 1-ethylcyclohexene (**66**) (Eq. 25).[85] Even though **66** has three allylic methylene groups, the reaction

is highly site selective for the least crowded of the three sites, forming ester **67** in 46% yield. Less than 5% of isomeric C–H insertion products are formed.



66 **67** (46%), dr 73:27 94% ee (Eq. 25)

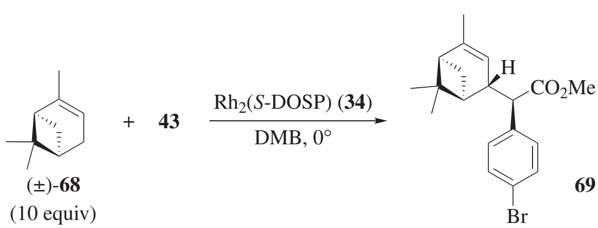
The reaction of catalyst **34** with (+)-α-pinene ((+)-**68**) illustrates an interesting case of catalyst-controlled diastereoselectivity (Eq. 26).[85] The Rh_2(*S*-DOSP)$_4$ (**34**) catalyzed reaction of (+)-**68** with aryldiazoacetate **43** affords predominantly diastereomer **69**. In contrast, the reaction with Rh_2(*R*-DOSP)$_4$ (*ent*-**34**) generates another diastereomer **70** with low diastereoselectivity. Furthermore, when the reaction is conducted with racemic α-pinene ((±)-**68**), kinetic resolution is observed, and diastereomer **69** is predominantly formed in 52% yield, 88:12 dr, and 99% ee (Eq. 27).[85]



(+)-**68** (0.5 equiv) **69** **70**

Rh catalyst	**69** + **70**	**69**:**70**
Rh_2(*S*-DOSP)$_4$ (**34**)	(93%)	98:2
Rh_2(*R*-DOSP)$_4$ (*ent*-**34**)	(62%)	24:76

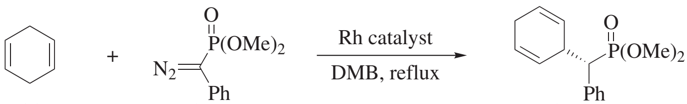
(Eq. 26)



(±)-**68** (10 equiv) **69** (52%), dr 88:12 99% ee (Eq. 27)

When the acceptor group of the diazo compound is not carbomethoxy, the ability of Rh_2(S-DOSP)$_4$ (**34**) to achieve high enantioselectivity in the C–H insertion reaction is generally diminished. In these instances, an excellent alternative catalyst is Rh_2(*S*-PTAD)$_4$ (**36**) as illustrated in Eq. 28.[111] The Rh_2(*S*-DOSP)$_4$ (**34**)-catalyzed insertion into 1,4-cyclohexadiene (**31**) with diazophosphonate **71** generates phosphonate **72** in only 41% ee, whereas use of catalyst **36** leads to phosphonate **72** in 92% ee. The two catalysts give opposite asymmetric induction

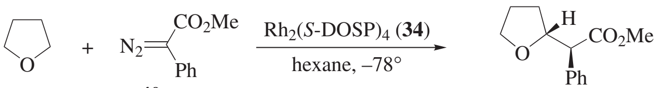
with the reactions of diazophosphonate **71**.



31 **71** **72** (Eq. 28)

Rh catalyst	Product		% ee
Rh_2(*S*-DOSP)$_4$ (**34**)	*ent*-**72**	(62%)	41
Rh_2(*S*-PTAD)$_4$ (**36**)	**72**	(83%)	92

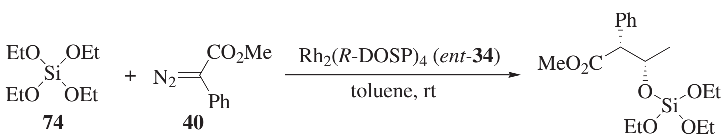
C–H Insertion α *to Oxygen*. The insertion into the C–H bond geminal to an oxygen substituent is generally favorable and can be achieved with all three major classes of metal carbenoids. Reaction of aryldiazoacetate **40** with tetrahydrofuran at −78° generates C–H insertion product **73** as a 4:1 mixture of diastereomers, in which the major diastereomer is obtained in 97% ee (Eq. 29).[53] Competition studies conducted at room temperature show that tetrahydrofuran is 2000 times more reactive than cyclohexane toward C–H insertion.



40 **73** (67%), dr 80:20 97% ee

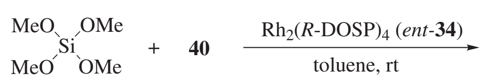
(Eq. 29)

Tetraalkoxysilanes are exceptional substrates for C–H insertion and are capable of highly diastereoselective reactions.[82] An impressive example is the reaction of aryldiazoacetates with tetralkoxysilanes shown in Eq. 30.[82] Rh_2(*R*-DOSP)$_4$ (*ent*-**34**)-catalyzed reaction of phenyl diazoacetate **40** with tetraethoxysilane (**74**) generates C–H insertion product **75** in 72% yield, 96% ee and >95:5 dr. The reactions of tetralkoxysilanes further demonstrate the balance between steric and electronic effects. Even though a range of alkoxysilanes containing secondary C–H bonds can be functionalized, tetramethoxysilane (**76**) is unreactive and tetraisopropoxysilane (**77**) gives a very low yield of C–H insertion product. Competition studies between tetramethoxysilane, tetraethoxysilane, and tetraisopropoxysilane reveal the enhanced reactivity of tetraethoxysilane, which is the only substrate that is functionalized (Eqs. 31 and 32).[82]

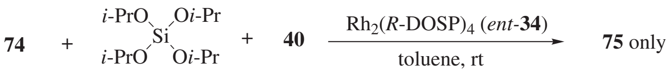


74 **40** **75** (70%), dr >95:5 96% ee

(Eq. 30)



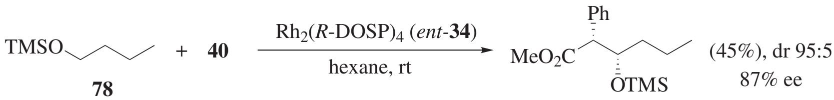
74 + **76** + **40** → **75** only (Eq. 31)



77

(Eq. 32)

The C–H functionalization can also be conducted on silyl ethers lacking any other functionality. The TMS derivative of butanol (**78**) undergoes C–H insertion to form ester **79** in 45% yield (Eq. 33).[90] Again, both diastereoselectivity and enantioselectivity are high. TMS ethers are preferred substrates because compounds with larger silyl groups are considerably less reactive.[90] For example, TIPS-protected butanol is 100 times less reactive than its TMS analog **78**.

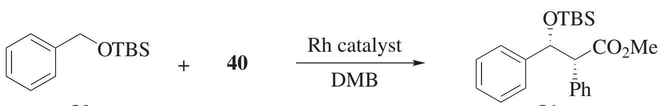


78

79

(Eq. 33)

In most instances, aryldiazoacetates give predictably high levels of enantiocontrol with Rh_2(*S*-DOSP)$_4$ (**34**). In some reactions, when the C–H insertion site is sterically crowded, the enantioselectivity can be reduced. An example of this is the reaction with aryl silyl ethers (Eq. 34).[112] Even though these systems give a high yield of product with good diastereocontrol, the Rh_2(*R*-DOSP)$_4$ (*ent*-**34**) catalyzed reaction of silyl ether **80** with methyl phenyldiazoacetate (**40**) gives C–H insertion product **81** in only 17% ee. A better catalyst for this reaction is the phthalimidocarboxylate complex Rh_2(*S*-PTTL)$_4$ (**37**), which leads to product **81** in 98% ee.[112]



80

81

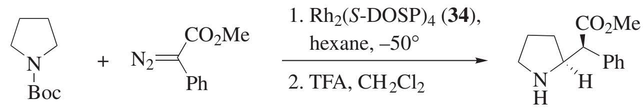
(Eq. 34)

Rh catalyst		dr	% ee
Rh_2(*R*-DOSP)$_4$ (*ent*-**34**)	(83%)	95:5	17
Rh_2(*S*-PTTL)$_4$ (**37**)	(95%)	>98:2	98

C–H Insertion α *to Nitrogen.* Insertion into a C–H bond geminal to a nitrogen substituent is another highly favorable process. For this transformation to be successful, the nitrogen needs to be suitably protected because N–H bonds are very prone to insertion by the carbenoid via ylide intermediates.[31] The nitrogen lone pair needs to be electronically or sterically protected or it can act as a nucleophile, coordinating to rhodium or attacking the electrophilic carbenoid. *N*-Boc[80,88,92,96] and *N*-aryl[98] groups are effective at electronically deactivating the nitrogen lone pair, whereas *N*,*N*-bis-silyl groups[105] sterically prevent attack by the carbenoid.

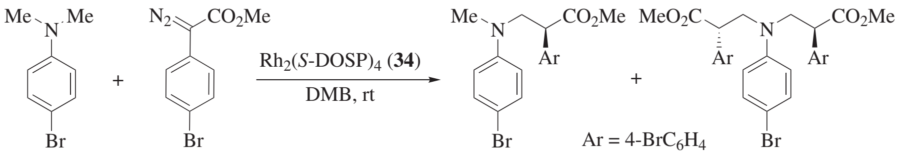
The *N*-Boc group plays an interesting role in carbenoid C–H insertion reactions; it not only protects the nitrogen from direct reaction with the carbenoid,

but it also has a significant steric influence. The reaction of aryldiazoacetate **40** with *N*-Boc-pyrrolidine (**82**) to yield ester **83** as shown in Eq. 35 is an illustrative example.[92]



82 + **40** → **83** (69%), dr 96:4, 94% ee (Eq. 35)

N,*N*-Dimethylanilines are excellent substrates for intermolecular C–H insertions. The aniline must be at least *para*-substituted to avoid attack of the carbenoid on the aromatic ring.[98] If diazoester **43** is the limiting reagent in the reaction with *N*,*N*-dimethylaniline (**84**), mono-insertion product **85** is formed in 72% yield, but if an excess of **43** is used, bis-insertion product **86** is formed in 60% yield (Eq. 36).[98] The second C–H insertion increases the enantioselectivity from 56% ee for mono-insertion product **85** to 90% ee for bis-insertion product **86**. The second C–H insertion event occurs with the same sense of asymmetric induction as the first, thus converting the major enantiomer of **85** into **86**. The minor enantiomer of **85** is converted into the *meso* diastereomer of **86**.

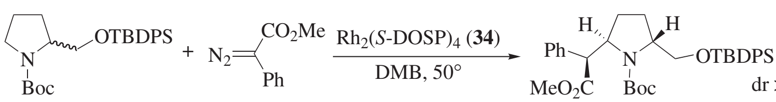


84 + **43** (*x* equiv) → **85** + **86**

x	**85**	% ee **85**	**86**	% ee **86**
0.5	(72%)	56	(—)	—
3.0	(—)	—	(60%)	90

(Eq. 36)

The complementary steric and electronic influences on the C–H insertion can be orchestrated to allow selective C–H functionalization of fairly elaborate systems. This behavior can be seen in the kinetic resolution of 2-substituted pyrrolidines as illustrated in Eq. 37.[92] Substrate **87** has three sites that have electronically activated C–H bonds, the C-2 and C-5 α to nitrogen, and the side-chain carbon α to oxygen. Two of these are sterically crowded, leaving only the C-5 position susceptible to C–H functionalization. Furthermore, when the reaction of pyrrolidine **87** with diazo compound **40** as the limiting agent is catalyzed by $Rh_2(S\text{-DOSP})_4$ (**34**), only one of the two enantiomers of **87** is reactive, resulting in the formation of stereoisomer **88** in 98% ee.



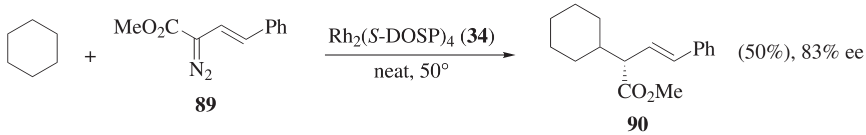
87 + **40** (0.5 equiv) → **88** (62%), dr >97:3, 98% ee

(Eq. 37)

Donor/Acceptor Carbenoids Derived from Vinyldiazoacetates

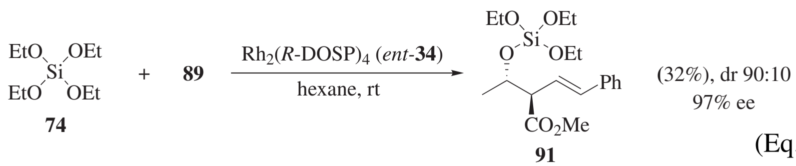
Donor/acceptor carbenoids derived from vinyldiazoacetate derivatives exhibit much richer chemistry than the carbenoids derived from aryldiazoacetates because the vinyl group can become an additional site of reactivity. The vinylcarbenoids are capable of undergoing C−H insertions, but when the reactions occur at allylic sites, the combined C−H activation/Cope rearrangement takes place.[41]

Reaction with Hydrocarbons. Only a few reactions of a vinyldiazoacetate with a hydrocarbon have been reported. The Rh_2(*S*-DOSP)$_4$ (**34**) catalyzed reaction of styryldiazoacetate **89** with cyclohexane results in the formation of C−H insertion product **90** in 50% yield and 83% ee (Eq. 38).[53]



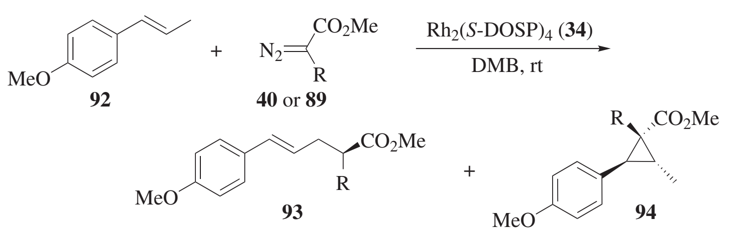
(Eq. 38)

Reaction with Activated C−H Bonds. A few examples of direct C−H insertion between vinyldiazoacetates and substrates bearing activated C−H bonds have been reported. The Rh_2(*R*-DOSP)$_4$ catalyzed reaction of styryldiazoacetate **89** with tetraethoxysilane (**74**) results in the formation of C−H insertion product **91** with 90:10 dr and 97% ee but in low yield (Eq. 39).[82]



(Eq. 39)

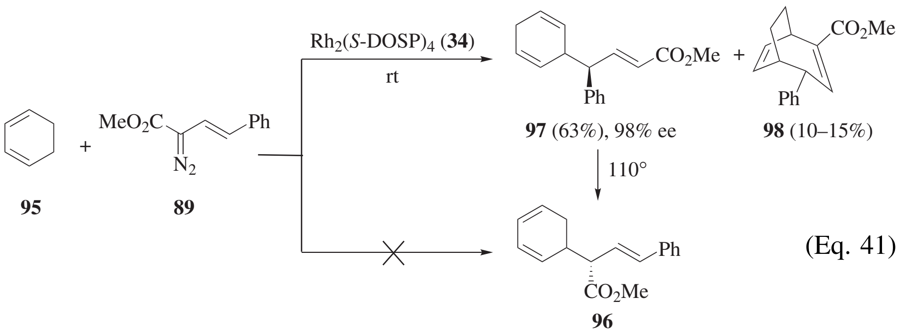
Another example that illustrates the difference between aryldiazoacetates and vinyldiazoacetates is the reaction with *p*-anethole (**92**) (Eq. 40).[109] The Rh_2(*S*-DOSP)$_4$ catalyzed reaction with styryldiazoacetate **89** gives exclusively cyclopropane **94b**, whereas the reaction with aryldiazoacetate **40** gave a mixture of cyclopropane **94a** and C−H insertion product **93a**.



(Eq. 40)

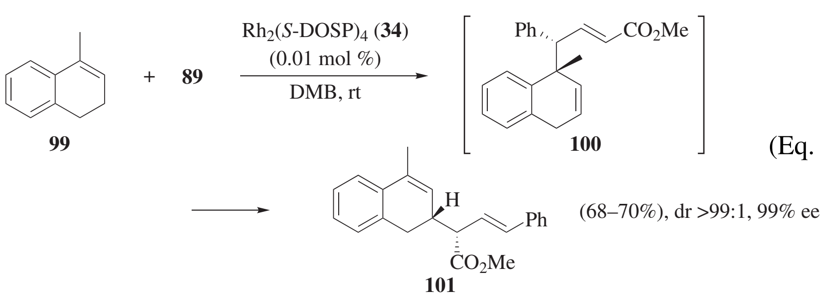
Carbenoid	R	Product	**93**	% ee **93**	**94**	% ee **94**
40	Ph	**93a**, **94a**	(53%)	91	(8%)	80
89	CH=CHPh	**93b**, **94b**	(—)	—	(61%)	74

The reaction of vinyldiazoacetates at allylic C–H bonds results in the "combined C–H activation/Cope rearrangement."[41] The combination of styryldiazoacetate **89** with 1,3-cyclohexadiene (**95**) is the first reported example of this reaction (Eq. 41).[81] No direct C–H insertion product **96** is formed. Instead the major product is 1,4-cyclohexadiene **97** along with a 10–15% yield of bicyclic compound **98**, which is derived from a tandem cyclopropanation/Cope rearrangement. Remarkably, product **97** is produced with 98% ee. Although the reaction appears to occur via a C–H insertion followed by a Cope rearrangement, this mechanism has been ruled out because C–H insertion product **96** is the thermodynamically more stable product, and thus cannot be an intermediate on the way to 1,4-cyclohexadiene **97**.[81]



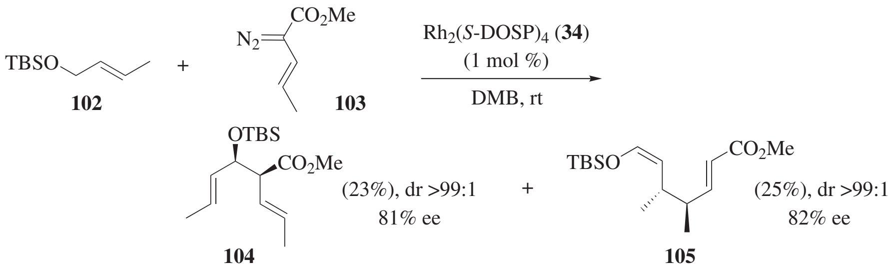
(Eq. 41)

One of the challenges with developing the combined C–H activation/Cope rearrangement has been to identify allylic substrates that are not susceptible to a competing direct C–H insertion. Dihydronaphthalenes work especially well as illustrated in Eq. 42. The reaction of styryldiazoacetate **89** with 4-methyl-1,2-dihydronapthalene (**99**) generates combined C–H activation/Cope rearrangement product **100** as a single diastereomer.[97] Because of the steric congestion, **100** is particularly prone to undergo a Cope rearrangement back to the product of direct insertion (**101**). The overall transformation proceeds with very high diastereo- and enantiocontrol (>99:1 dr, 99% ee). The direct C–H insertion does not result in such high levels of stereocontrol. Catalyst loadings as low as 0.01 mol % can be employed for the large-scale preparation of product **101**.[110]



(Eq. 42)

Allyl silyl ethers are good substrates for the combined C–H activation/Cope rearrangement.[95] As illustrated by the reaction of 2-diazobutenoate **103** with allyl silyl ether **102** (Eq. 43), a mixture of C–H insertion product **104** and combined C–H insertion/Cope rearrangement product **105** is formed.[95] In this case, conversion of direct C–H insertion product **104** to rearrangement product **105** is thermodynamically favored by formation of both enoxysilane and conjugated ester functional groups. This rearrangement can be achieved by heating **104** in toluene.



(Eq. 43)

APPLICATIONS TO SYNTHESIS

New methods for C–H functionalization are of considerable interest because they offer new strategies for synthesis.[34,35] The intermolecular C–H insertions of metal carbenoids derived from aryldiazoacetates have been shown to complement a number of the classic reactions of organic synthesis. This concept is summarized in Fig. 6. C–H insertions of unactivated substrates can be considered as a synthetic equivalent of enolate alkylation (a).[53,116] The two approaches, however, are complementary because enolate alkylations are best performed on primary alkyl halides whereas the insertions are best conducted on secondary and tertiary C–H bonds. C–H insertion α to an oxygen substituent generates β-hydroxy esters, the products of a classic aldol reaction (b).[90] The C–H functionalization of ketals generates ketal-protected β-keto esters.[101] This reaction can be considered to complement the asymmetric Claisen condensation (c), a reaction that is not normally conducted asymmetrically because the unprotected β-keto esters are too prone to epimerization at the α position. C–H insertion α to nitrogen generates β-amino esters, normally the products of a Mannich reaction (d).[92] Allylic C–H insertion generates γ,δ-unsaturated esters,[85] the products of a Claisen rearrangement (e), whereas the reaction with silyl enol ethers generates protected 1,5-dicarbonyl products,[84,97] which are traditionally formed by Michael addition (f).

An illustration of how C–H insertion of alkanes complements enolate alkylation is the $Rh_2(S\text{-DOSP})_4$ catalyzed reaction of styryldiazoacetate **89** with adamantane (**106**) (Eq. 44).[111] C–H insertion product **107** is formed in 58% yield and 91% ee. Introduction of an adamantyl group by means of enolate alkylation is not practical because it would require a nucleophilic substitution at a tertiary alkyl halide. This C–H insertion reaction has been conducted on a 0.2-mole scale and allylic ester **107** can be enriched to >98% ee by means of

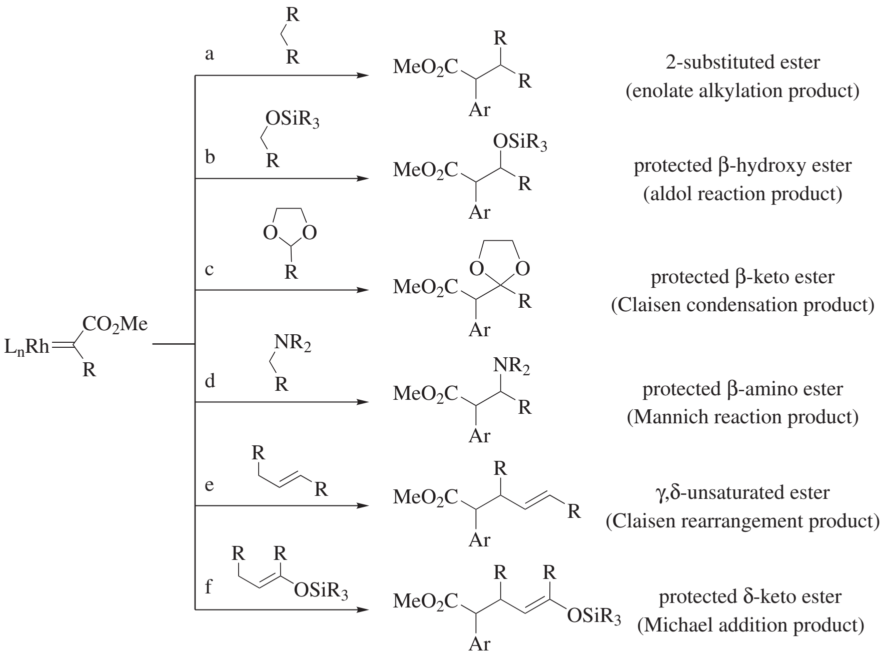
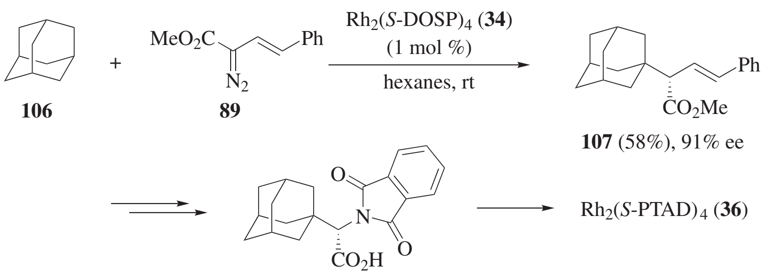


Figure 6. Complementary nature of C–H insertion reactions with respect to classic organic synthesis.

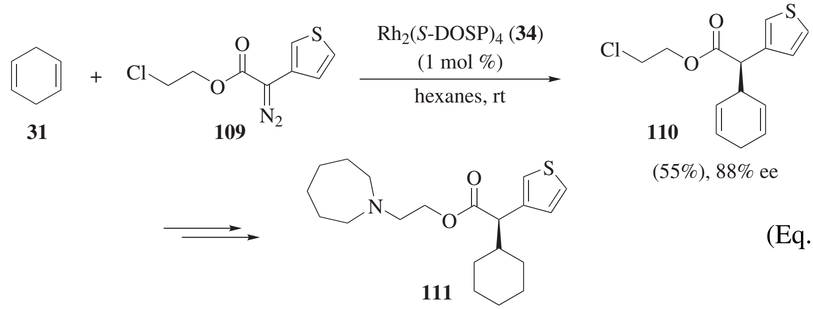
a single recrystallization. This process was used for the synthesis of adamantyl glycine derivative **108**, which was then incorporated into $Rh_2(S\text{-PTAD})_4$ **36**.[111]



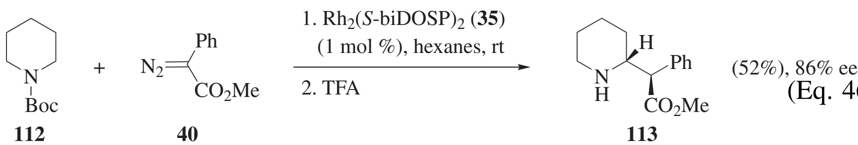
106 + **89** → **107** (58%), 91% ee → **108** (Eq. 44)

The C–H insertion by aryldiazoacetates has been applied to direct asymmetric syntheses of various pharmaceuticals. $Rh_2(S\text{-DOSP})_4$ (**34**)-catalyzed reaction of thienyldiazoacetate **109** with 1,4-cyclohexadiene **31** generates ester **110** in 55% yield (Eq. 45).[89] Catalytic hydrogenation followed by a nucleophilic substitution completes the synthesis of acetyl cholinesterase inhibitor cetiedil (**111**). The reaction of phenyldiazoacetate **40** with N-Boc-piperidine (**112**) followed by acid-induced deprotection constitutes a rapid approach to *threo*-methylphenidate (**113**,

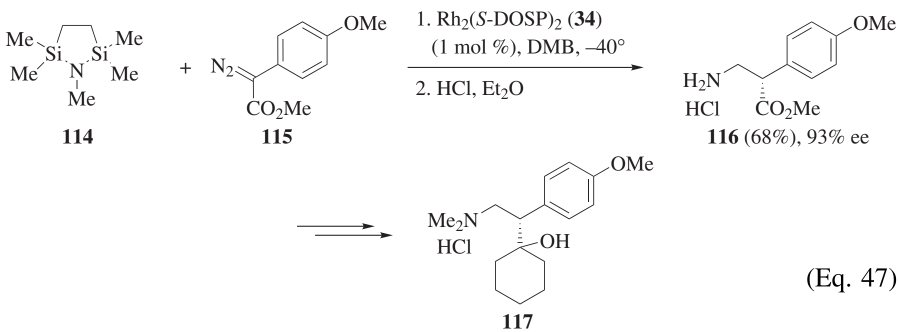
Ritalin), a currently marketed drug for treatment of attention deficit hyperactivity disorder (Eq. 46).[80,92,115] An effective catalyst in this case is the bridged prolinate catalyst Rh_2(*S*-biDOSP)$_2$ (**35**),[80,92] although chiral rhodium carboxamidates are also successfully employed in this reaction.[115] The reaction of bis silyl protected methylamine **114** with aryldiazoacetate **115** is an effective method for synthesizing β-amino acid **116** (Eq. 47).[105] Dimethylation of **116** followed by reaction with a bis-Grignard reagent results in the formation of the antidepressant venlafaxine (**117**).



(Eq. 45)

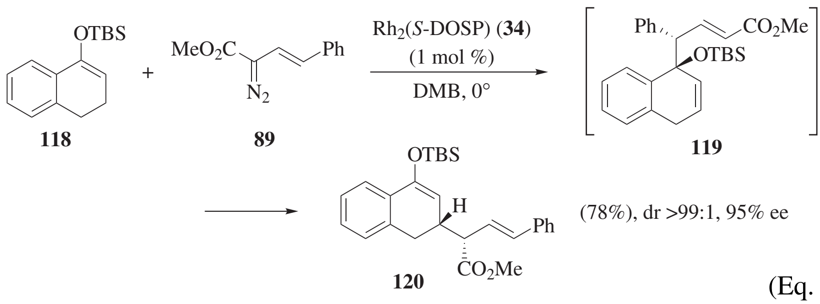


(Eq. 46)



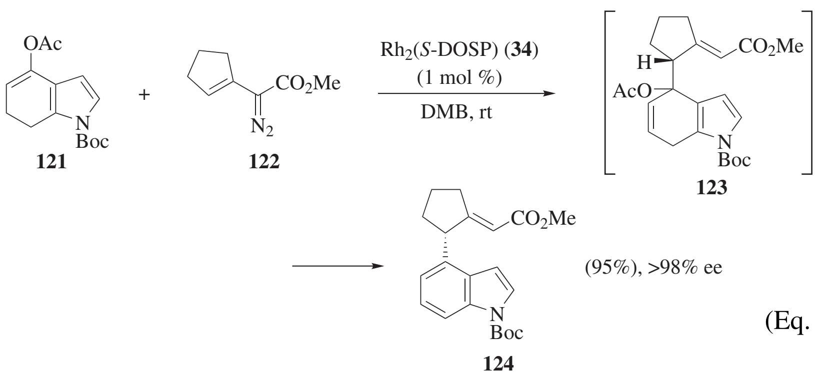
(Eq. 47)

The combined C–H activation/Cope rearrangement has been used, for example, in the reaction between styryldiazoacetate **89** and silyloxydihydronaphthalene **118**. This is an intriguing reaction because C–H activation/Cope rearrangement product **119** undergoes a retro-Cope rearrangement to yield allylic ester **120**, the product formally arising from direct C–H insertion (Eq. 48).[97] However, **120** is formed in 95% ee and >99:1 dr, much higher stereoselectivities than what would be expected from a direct C–H insertion.



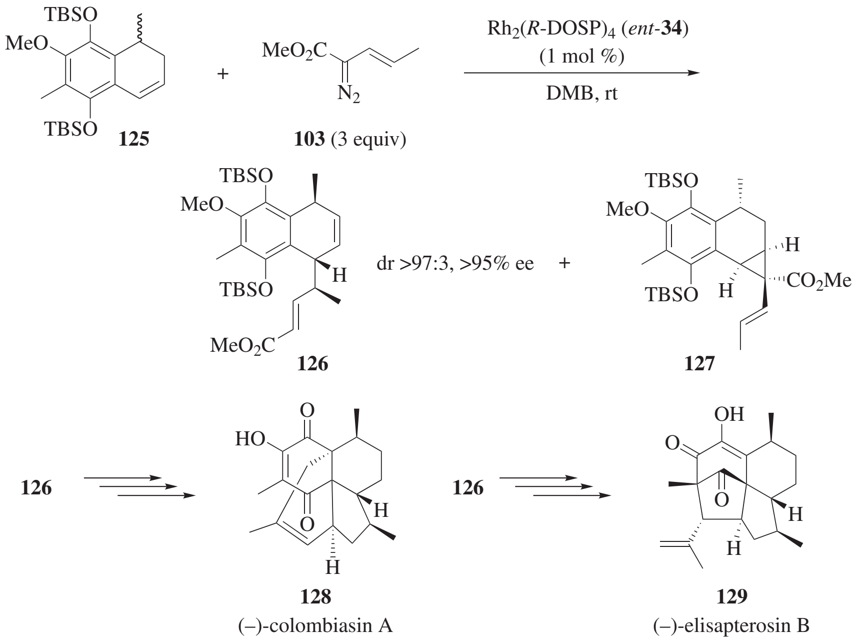
(Eq. 48)

Another illustration is the reaction of vinyldiazoacetate **122** with dihydroindole **121** (Eq. 49).[104] The first step is the combined C–H activation/Cope rearrangement to form product **123**, which then aromatizes by loss of acetic acid to generate 4-substituted indole **124**. This reaction has been employed with a variety of vinyldiazoacetates to form 4-substituted indoles with 97–99% ee.



(Eq. 49)

The combined C–H activation/Cope rearrangement has also been applied to the synthesis of a range of marine diterpene natural products (Eq. 50).[100,102,103,108] The key step is an enantiodivergent carbenoid reaction on racemic 1-methyl-1,2-dihydronaphthalenes. Under $Rh_2(S\text{-DOSP})_4$ (**34**) catalyzed conditions, one enantiomer of dihydronaphthalene **125** undergoes a combined C–H activation/Cope rearrangement to form product **126**, whereas the other enantiomer undergoes cyclopropanation to form product **127**.[103] Thus, three stereogenic centers in these marine natural products are set up in one step. In a few steps, ester **126** is converted into colombiasin A (**128**) and elisapterosin B (**129**). This type of enantiodifferentiation reaction has been applied to other dihydronaphthalenes, leading to the synthesis of several other natural products.[100,102,108]

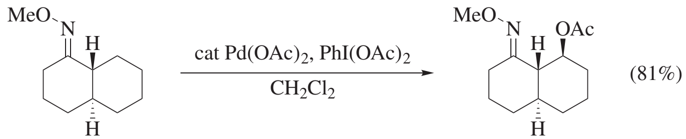


(Eq. 50)

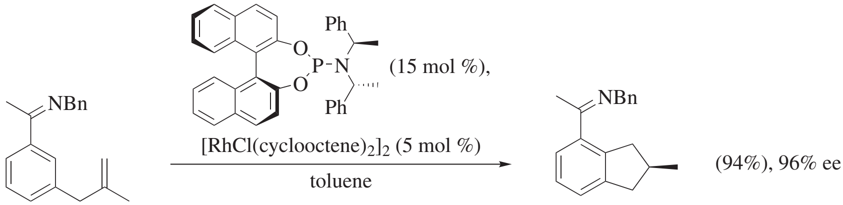
COMPARISON WITH OTHER METHODS

Intermolecular C–H insertions offer surrogate approaches to some of the classic reactions of organic synthesis. As discussed in the previous section, in many instances the carbenoid C–H insertion strategy is complementary to the conventional process. With certain substrates, the C–H insertion can be highly diastereo- and enantioselective and can be conducted with low chiral catalyst loading, making the process a viable alternative to conventional synthetic methods.

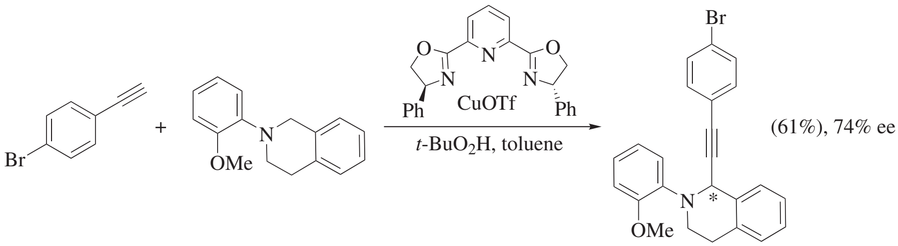
C–H functionalization is a rapidly growing field in organic synthesis.[35,42,117–124] Two distinct organometallic approaches are used to achieve C–H functionalization. One is an outer-sphere process, and the carbenoid C–H insertion approach belongs to this class of reaction. The other is an inner sphere process, in which the metal initially inserts into the C–H bond. Site selectivity is an obvious challenge for both types of C–H functionalization. In the metal C–H insertion, the most effective strategy to achieve this selectivity has been to have a neighboring group to direct the metal toward the C–H insertion site.[117] Once the metal has inserted into the C–H bond, further transformations can be conducted to generate synthetically useful organic products. Illustrative examples of the types of transformations that can be achieved are shown in Eqs. 51–53.[125,126] The inner sphere C–H functionalization is complementary to the carbenoid reaction because even though they both involve a C–H insertion step, they lead to different types of products.



(Eq. 51)

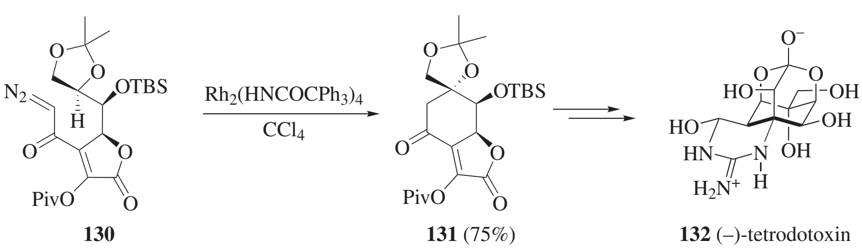


(Eq. 52)



(Eq. 53)

Intramolecular C–H insertion is an important alternative to intermolecular C–H insertion.[32,43,127] Due to the challenges in achieving site selectivity in the early examples of intermolecular C–H insertions, intramolecular variants were developed to control the chemistry. By now, a range of chiral catalysts have been developed for asymmetric intramolecular C–H insertions, allowing the transformation to be applied to the synthesis of a number of natural products.[128–131] One of the most impressive recent examples is a key step in the synthesis of tetrodotoxin (**132**) (Eq. 54).[132] Compound **130** contains a number of reactive sites for C–H insertion, but by conducting the reaction intramolecularly, a clean transformation is obtained to form product **131**.



(Eq. 54)

The decision to conduct a C–H insertion in an inter- or intramolecular fashion depends on several factors. Certainly, intramolecular C–H insertion is likely to give better site selectivity, but a disadvantage with this approach is the synthesis of the substrate and the choice of the tether. The synthesis of imperanene (**133**) provides a good illustration of the competing factors because it has been accomplished by both inter-[91] and intramolecular[127] routes (Fig. 7). The C–H insertion step proceeds in higher yield in the intramolecular reaction, but the synthesis of the substrate and the completion of the synthesis require far more steps than the intermolecular approach.

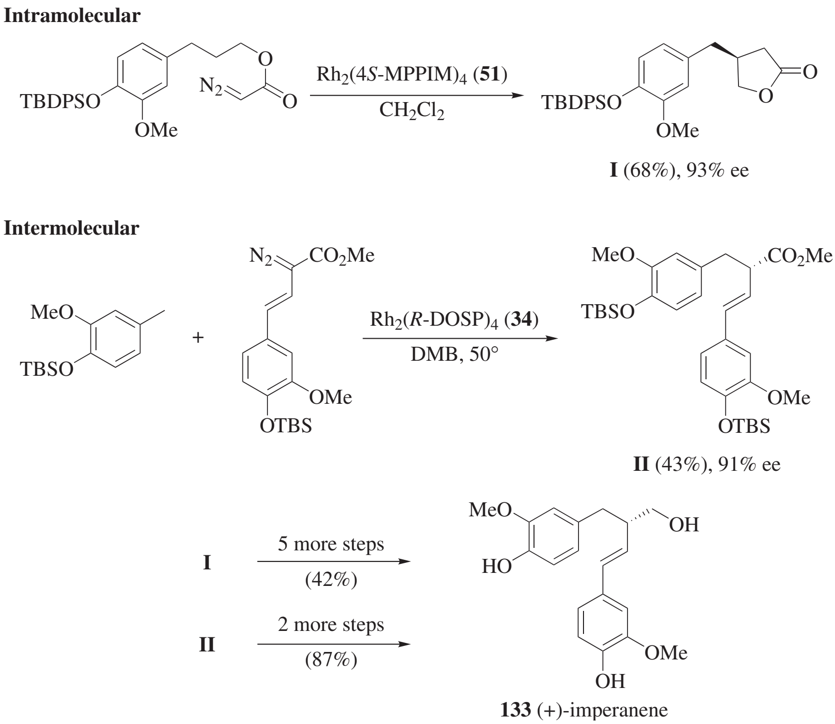


Figure 7. Intramolecular vs. intermolecular C–H insertion towards the total synthesis of (+)-imperanene.

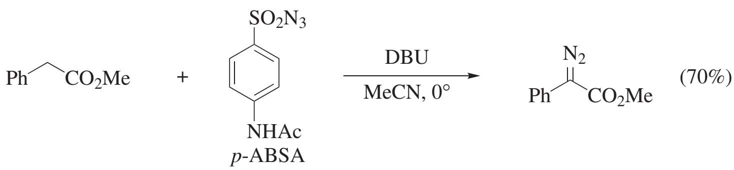
EXPERIMENTAL CONDITIONS

Intermolecular C–H insertions should be carried under an inert atmosphere using anhydrous conditions. The reactions are usually carried out by the dropwise addition of a solution of the requisite diazo compound to a stirred solution of the catalyst and substrate. Typical catalysts for these types of transformations are copper(I) complexes, metal porphyrins, and rhodium(II) carboxylates and carboxamidates. Rhodium(II) catalysts are stable to open atmosphere, whereas

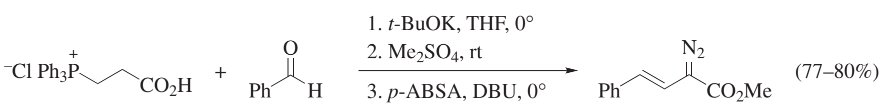
the copper(I) complexes and metal porphyrins are generated in situ from stable precursors.

Warning: *Great care should be taken in the handling of diazo compounds due to their explosive properties and toxicity potential. Diazo compounds should be handled carefully and all reactions should be carried out in a well-ventilated fume hood. Careful risk assessment analysis should be conducted before running large-scale reactions of diazo compounds.* For a detailed discussion on the handling of diazo compounds, see a previous *Organic Reactions* review.[33]

EXPERIMENTAL PROCEDURES

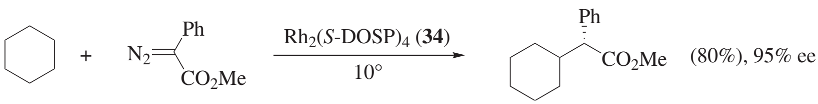


Methyl Phenyldiazoacetate [Diazo Transfer Reaction Using 4-Acetamidobenzenesulfonyl Azide].[53] (*p*-ABSA is available commercially and is a safer alternative to more traditional diazotransfer agents such as toluenesulfonyl azide.) Methyl phenyl acetate (1 equiv, 5–100 mmol) and *p*-ABSA (1.2 equiv) were dissolved in MeCN and cooled to 0° under an Ar atmosphere. DBU (1.2 equiv) was added in one portion to the stirred mixture, the ice bath was removed and the mixture was stirred for 2–4 h under Ar. The reaction was quenched with saturated aqueous NH_4Cl solution and the water layer was extracted with Et_2O (3×). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was triturated with 50% Et_2O/50% petroleum ether, the solid was removed by filtration and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (98% petroleum ether/2% Et_2O) to give the title product (70% yield): IR (neat) 3025, 2952, 2083, 1704, 1503, 1437, 1355, 1251, 1156, 1053, 756, 693 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.7 Hz, 2H), 7.47 (t, J = 8.3 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 3.87 (s, 3H). Anal. Calcd for $C_9H_8N_2O_2$: C, 61.36; H, 4.58. Found: C, 61.28; H, 4.54.

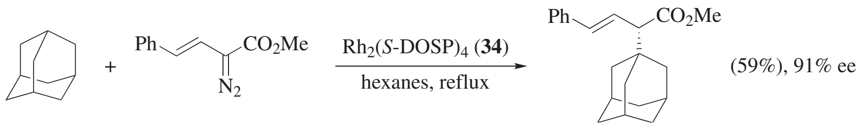


Methyl (*E*)-2-Diazo-4-phenyl-3-butenoate [One-Pot Preparation of a Vinyldiazoacetate from an Aromatic Aldehyde].[110] 2-Carboxyethyltriphenylphosphonium chloride (26.7 g, 72.0 mmol) was added to a flame-dried, 2-necked 500 mL round-bottomed flask equipped with a magnetic stir bar and fitted with a rubber septum and an argon inlet adapter. The flask was alternatively evacuated

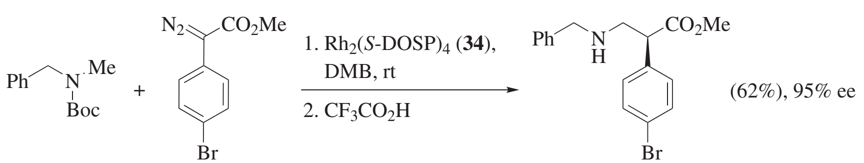
and filled with argon twice, after which a positive argon pressure was maintained on the flask. Benzaldehyde (6.07 mL, 60.0 mmol) and THF (130 mL) were then added by syringe while the flask was externally cooled to 0° in an ice-water bath. A solution of potassium *tert*-butoxide (16.8 g, 150 mmol) in THF (80 mL) was added via cannula over 30 min. After the addition was complete, the solution was stirred at 0° for 30 min, then the ice-water bath was removed and the stirring was continued for another 20 min. Dimethyl sulfate (11.4 mL, 120 mmol) was then added rapidly by syringe and stirring was continued at rt for 2.5 h. 4-Acetamidobenzenesulfonyl azide (18.7 g, 78.0 mmol) was then added in one portion and the flask was externally cooled to 0° in an ice-water bath. DBU (11.7 mL, 78.0 mmol) was added rapidly, and the solution quickly turned red. Stirring was continued at 0° for 4 h and the mixture was warmed to rt. The solution was concentrated by rotary evaporation. The residue was treated with saturated aqueous NH_4Cl solution (150 mL) and Et_2O (400 mL) and the mixture poured into a 1-L separatory funnel and vigorously shaken. The aqueous layer was drained and the organic layer was washed with saturated aqueous NH_4Cl solution (150 mL) and dried over anhydrous $MgSO_4$. The residue was purified by silica gel chromatography (350 g) using 92% pentane/8% Et_2O as the eluent, to afford the title product (9.3–9.7 g, 77–80% yield) as a red solid: IR (neat) 3010, 2940, 2040, 1695, 1620, 1590, 1440 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.15 (m, 5 H), 6.44 (d, J = 16.2 Hz, 1 H), 6.15 (d, J = 16.2 Hz, 1 H), 3.81 (s, 3 H).



Methyl (*R*)-α-Cyclohexylphenylacetate [Reaction of an Aryl-Derived Donor/Acceptor-Substituted Carbenoid with a Hydrocarbon].[53] A degassed solution of methyl phenyldiazoacetate (1 mmol) in anhydrous cyclohexane (10 mL) was added dropwise over 90 min to a stirred, degassed solution of Rh_2(*S*-DOSP)$_4$(**34**, 0.01 mmol) in anhydrous cyclohexane (5 mL) at 10°. The solution was stirred at 10° for an additional 15 min and then warmed to rt. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (98% petroleum ether/2% Et_2O) to afford the title product (80% yield): 95% ee (Chiralcel-OD, 99.4% hexane/0.6% 2-propanol, 1.0 mL/min, 254 nm; t_R = 8.6 and 10.4 min); $[\alpha]^{23}{}_D - 35.1°$ (*c* 0.57, $CDCl_3$); IR (neat) 3028, 2926, 2850, 1735, 1497 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 − 7.22 (m, 5 H), 3.64 (s, 3 H), 3.22 (d, J = 10.6 Hz, 1 H), 2.03–1.97 (m, 1 H), 1.81–1.56 (m, 4 H), 1.32–1.01 (m, 5 H), 0.87–0.70 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 174.4, 137.9, 128.6, 128.4, 127.2, 58.8, 51.7, 41.0, 32.0, 30.4, 26.2, 25.94, 25.90.

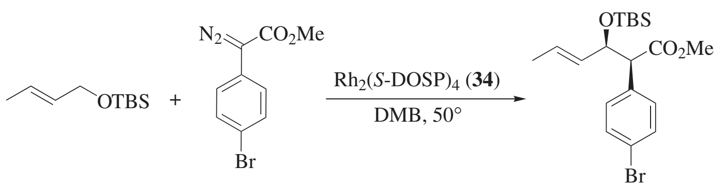


(S)-(E)-Methyl 2-Adamantyl-4-phenylbut-3-enoate [Reaction of a Vinyl-Derived Donor/Acceptor-Substituted Carbenoid with a Hydrocarbon].[111] To a flame-dried, 2-L round-bottomed flask under argon and charged with a magnetic stir bar was added adamantane (141.1 g, 1.03 mol, 5 equiv) and $Rh_2(S\text{-DOSP})_4$ (**34**, 2.02 g, 0.5 mol %) dissolved in 700 mL of degassed hexanes. This solution was heated to reflux. A solution of methyl styryldiazoacetate (42 g, 0.21 mol) in degassed hexanes (200 mL) was then added to this refluxing solution via cannula over 45 min. Once the addition was completed the mixture was allowed to reflux for 2 h. After cooling, the mixture was stirred for 2 h at rt. The solvent was then removed under vacuum and excess adamantane was removed by Kugelrohr distillation. The residue was purified by silica gel chromatography (5:1 hexanes/EtOAc) to give the title product (39.6 g, 59% yield, 91% ee) as a white solid. The product was recrystallized from methanol (740 mL) to give the enantiomerically enriched product (36.4 g, 92% recovery, >99% ee) as a white solid: mp 115–117°; R_f 0.5 (4:1 hexanes/EtOAc); $[\alpha]_D^{25}$ – 74.9° (*c* 1.0, $CHCl_3$); FTIR (neat) 3023, 2924, 2850, 1725, 1598, 1497, 1454, 1346, 1317, 1260, 1149, 1190, 999, 754, 692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.21 (t, J = 7.5 Hz, 1H), 6.35 (m, 2H), 3.67 (s, 3H), 2.79 (d, J = 8.5 Hz, 1H), 1.97 (s, 3H), 1.77–1.51 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 136.8, 133.4, 128.5, 127.4, 126.3, 124.8, 61.4, 51.2, 40.1, 36.7, 36.3, 28.6. Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25, H, 8.44. Found: C, 81.34; H, 8.32. HPLC analysis (Chiralpak AD-RH, 99% hexanes/1% 2-propanol, 0.5 mL/min, 254 nm; t_R (major) = 8.8 min; t_R (minor) = 10.5 min): 91% ee before recrystallization and >99% ee after one recrystallization.



3-Benzylamino-(2S)-(4-bromophenyl)propionic Acid Methyl Ester [C–H Insertion Adjacent to a Nitrogen Substituent].[88] Methyl 4-bromophenyldiazoacetate (230 mg, 0.90 mmol) in 2,2-dimethylbutane (7 mL) was added dropwise over 3 h using a syringe pump to a solution of $Rh_2(S\text{-DOSP})_4$ (**34**, 17 mg, 0.01 mmol) and *N*-benzyl-*N*-methylcarbamic acid *tert*-butyl ester (100 mg, 0.45

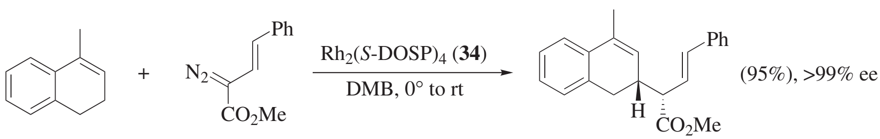
mmol) in 2,2-dimethylbutane (5 mL). After the addition, the resulting solution was stirred at rt for 1 h. The solvent was removed under reduced pressure and the residue was redissolved in CH_2Cl_2 (10 mL) and TFA (0.2 mL, 2.26 mmol) and the solution was stirred for 16 h at rt. The solution was concentrated under vacuum, and the residue was dissolved in Et_2O (20 mL) and extracted with 10% HCl (3 × 15 mL). The combined aqueous layers were basified ($NaHCO_3$, 1 M NaOH to pH 8–9) and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with water (1 × 15 mL) and brine (1 × 20 mL) and then dried over Na_2SO_4. The product was purified by silica gel chromatography (25:35:2 Et_2O/pentane/NEt_3) to give the title compound (97 mg, 0.28 mmol, 62% yield): $[\alpha]^{25}{}_D$ − 44.71° (*c* 1.36, $CHCl_3$); IR (neat): 3328, 3024, 2948, 2844, 1730, 1490, 1455, 1163, 1011 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.5 Hz, 2H), 7.32–7.22 (m, 5H), 7.16 (d, *J* = 7.0 Hz, 2H), 3.80 (s, 2H), 3.77 (m, 1H), 3.66 (s, 3H), 3.26 (m, 1H), 2.91 (dd, *J* = 6.5, 11.5 Hz, 1H); ^{13}C NMR (DEPT) (125 MHz, $CDCl_3$) δ 173.1 (C), 139.8 (C), 136.1 (C), 131.8 (CH), 129.7 (CH), 128.3 (CH), 127.9 (CH), 126.9 (CH), 121.4 (CH), 53.5 (CH_2), 52.1 (CH_3), 51.7 (CH_2), 51.5 (CH). Anal. Calcd for $C_{17}H_{18}NBrO_2$: C, 58.63; H, 5.21; N, 4.02. Found: C, 58.76; H, 5.25; N, 4.06. To measure the enantiomeric excess of the above compound, it was converted to its trifluoroacetamide. Acylation of a small sample of the free amine from above with TFAA and CH_2Cl_2 followed by silica gel chromatography (85% pentane/15% Et_2O) gave the amide in 95% ee (HPLC, Chiralcel-AD-RH, 95.0% hexanes/5.0% 2-propanol, 1.0 mL/min, 1 mg/mL, 254 nm; t_R (major) = 4.62 min; t_R (minor) = 8.16 min): IR (neat) 3041, 2948, 1735, 1691, 1210, 1166, 1144 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.37–7.32 (m, 3H), 7.13–7.10 (m, 4H), 4.65 (s, 3H), 4.24 (m, 2H), 3.87–3.77 (m, 1H), 3.68 (s, 3H), 3.52–3.48 (dd, *J* = 7.0 Hz, 13.5 Hz, 1H); EI-MS *m/z* (relative intensity): [M^+] 443 (1%), 346, 240.



(71%), dr >97:3
68% ee

(2*S*,3*R*)-(*E*)-Methyl 2-(4-Bromophenyl)-3-(*tert*-butyldimethylsiloxy)hex-4-enoate [C–H Insertion Adjacent to an Oxygen Substituent].[90] Methyl 4-bromophenyldiazoacetate (0.79 mmol) in 2,2-dimethylbutane (7.9 mL) was added dropwise over 45 min via a syringe pump to a rapidly stirred solution of allylic silyl ether (0.39 mmol) and Rh_2(*S*-DOSP)$_4$ (**34**, 15 mg, 0.0079 mmol) in 2,2-dimethylbutane (1.0 mL) at 50°. On completion of the addition, the reaction

mixture was allowed to stir for an additional 15 min, followed by concentration under vacuum. Purification by silica gel chromatography (4:1 petroleum ether/CH_2Cl_2) afforded the title compound (118 mg, 71% yield) as a colorless oil with >97:3 dr (by ^{1}H NMR of the crude reaction mixture): $[\alpha]_D^{25}$ −20.5° (*c* 1.61, $CHCl_3$); IR (film) 2954, 2929, 2886, 2856, 1737, 1488, 1255, 1073, 837 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 5.65 (dq, $J = 15.5$, 6.5 Hz, 1H), 5.36 (ddd, $J = 15.5$, 7.5, 1.5 Hz, 1H), 4.52 (app t, $J = 8.0$ Hz, 1H), 3.63 (s, 3H), 3.54 (d, $J = 8.0$ Hz, 1H), 1.65 (dd, $J = 6.5$, 1.5 Hz, 3H), 0.70 (s, 9H), −0.12 (s, 3H), −0.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 135.4, 132.0, 131.3, 131.2, 128.1, 121.4, 75.7, 59.1, 51.9, 25.6, 18.0, 17.7, 4.2, −5.4; LRMS-ESI m/z (relative intensity): [M + Na] 435 (36%), 185 (100%); HRMS-FAB: [M + Na] calcd for $C_{19}H_{29}O_3BrNaSi$, 435.0962; found, 435.0958. HPLC analysis: 68% ee (Chiralcel-OD-H, 99.4% hexane/0.6% 2-propanol, 0.2 mL/min, 254 nm; t_R (major) = 23.3 min; t_R (minor) = 26.1 min). The reaction at rt gave the title product in 65% yield and 79% ee.



(*S*)-(*E*)-Methyl 2-((*R*)-4-Methyl-1,2-dihydronaphthalen-2-yl)-4-phenylbut-3-enoate [Combined C–H Activation/Cope Rearrangement Followed by a Retro-Cope Rearrangement].[97] To a solution of 4-methyl-1,2-dihydronaphthalene (0.5 mmol) and $Rh_2(S\text{-DOSP})_4$ (**34**, 0.0025 mmol) in 2,2-dimethylbutane (1 mL) was added a solution of methyl (*E*)-2-diazo-4-phenyl-3-butenoate (111 mg 0.55 mmol) in 2,2-dimethylbutane (5 mL) over 45 min via syringe pump at 0°. The resulting mixture was then stirred overnight at rt. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (20:1 to 10:1 pentane/Et_2O) to afford the title product (151 mg, 95% yield) as a white solid: mp 75–77°; $[\alpha]^{23}_D$−30.4° (*c* 4.10, $CHCl_3$); IR (neat) 3059, 3026, 2949, 1733, 1490, 1450, 1435, 1260, 1193, 1158, 1027 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.35–7.28 (m, 4H), 7.25–7.17 (m, 3H), 7.14 (td, $J = 7.0$, 1.8 Hz, 1H), 7.07 (d, $J = 7.0$ Hz, 1H), 6.41 (d, $J = 15.9$ Hz, 1H), 6.14 (dd, $J = 15.9$, 9.8 Hz, 1H), 5.73 (d, $J = 3.0$ Hz, 1H), 3.68 (s, 3H), 3.10 (t, $J = 9.3$ Hz, 1H), 2.87 (dd, $J = 14.2$, 6.0 Hz, 1H), 2.86–2.79 (m, 1H), 2.71 (dd, $J = 14.2$, 6.5 Hz, 1H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.6, 136.6, 135.2, 134.3, 133.61, 133.56, 128.5, 127.8, 127.7, 127.1, 126.5, 126.3, 126.2, 126.0, 123.0, 53.1, 51.8, 36.0, 31.6, 19.4. HPLC analysis: >99% ee (Chiralcel-OD-H, 98.0% hexane/2.0% 2-propanol, 0.8 mL/min, 254 nm; t_R = 9.2 and 10.9 min).

TABULAR SURVEY

Tables 1–5 cover the intermolecular C–H insertion reactions of the various carbenoid classes derived from diazo compounds. The charts appearing before the tables depict the structures of the catalysts used in the tabular survey. The tables cover the relevant literature reported through June 2008.

The tables are arranged in the same order as the topics are discussed in the Scope and Limitations section. C–H insertion reactions utilizing acceptor-substituted carbenoids derived from diazoesters are presented in Table 1. Reactions utilizing acceptor/acceptor-substituted carbenoids derived from diazoesters are presented in Table 2. Reactions of donor/acceptor-substituted carbenoids generated from aryldiazo (and heteroaryldiazo) derivatives are presented in Table 3 and those generated from vinyldiazo derivatives are presented in Table 4. Some miscellaneous diazo compounds that do not belong to the three major classes have been used in C–H functionalization and these results are presented in Table 5.

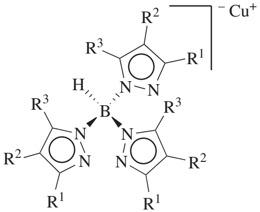
Entries in the tables are arranged in order of increasing carbon number of the C–H-bearing substrates. The carbon count is based on the total number of the carbon skeleton with the exception of nitrogen protecting groups. Yields of the products are given in parentheses. Unspecified yields are noted by (–). The term "ee" is used to describe the enantiomeric excess and "dr" is used to describe the diastereomeric ratio of a particular transformation product.

The following abbreviations are used in the tables:

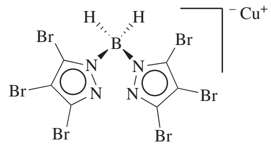
p-ABSA	*p*-acetamidobenzenesulfonyl azide
Ad	adamantyl
Alloc	allyloxycarbonyl
bipy	bipyridyl
bmim	1-butyl-3-methylimidazolium
BNP	binaphthyl phosphate
DBMP	2,6-di-*tert*-butyl-4-methylphenyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DMB	2,2-dimethylbutane
ee	enantiomeric excess
hfacac	hexafluoroacetylacetonate
NHC	*N*-heterocyclic carbene
Np	naphthyl
Oct	octanoate
pfb	perfluorobutyrate
PFMC	perfluoromethylcyclohexane
PG	protecting group
Phthal	phthalimide

TBDPS	*tert*-butyldiphenylsilyl
Teoc	2-trimethylsilylethyloxycarbonyl
TFT	trifluorotoluene
tol	tolyl, methylphenyl
TPA	triphenyl acetate

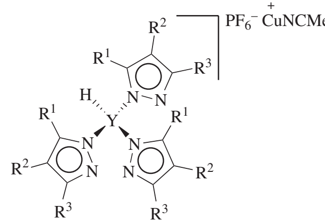
CHART 1. COPPER CATALYST COMPLEXES



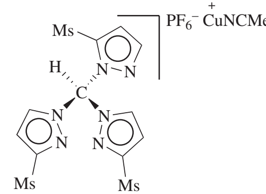
	R^1	R^2	R^3	
1:	H	H	H	TpCu
2:	Me	H	H	Tp*Cu
3:	Np	H	H	$Tp^{Np}Cu$
4:	Ms	H	H	$Tp^{Ms}Cu$
5:	Br	Br	Br	$Tp^{Br3}Cu$
6:	Cy	H	H	$Tp^{Cy}Cu$
7:	Ph	H	H	$Tp^{Ph}Cu$
8:	CF_3	H	CF_3	$Tp^{(CF3)2}Cu$



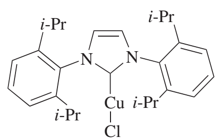
9 $Bp^{Br3}Cu$



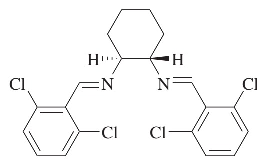
	Y	R^1	R^2	R^3	
10:	B	Br	Br	Br	$Tp^{Br3}Cu(NCMe)$
11:	C	Me	H	Me	$Tpm^{Me2}Cu(NCMe)$
12:	C	H	H	Ms	$Tpm^{Ms}Cu(NCMe)$



13 $Tpm^{Ms*}Cu(NCMe)$

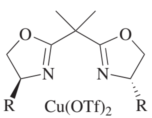


14 Cu(NHC1)

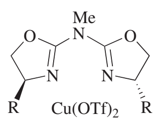


$(CuOTf)_2C_6H_6$

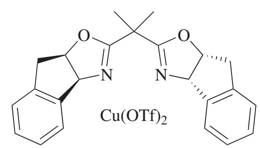
15 Cu(SALEN)



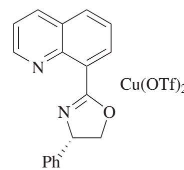
	R	
16:	Ph	Cu(BOX1)
17:	*t*-Bu	Cu(BOX2)
18:	*i*-Pr	Cu(BOX3)



	R	
19:	Ph	Cu(BOX4)
20:	*t*-Bu	Cu(BOX5)
21:	*i*-Pr	Cu(BOX6)

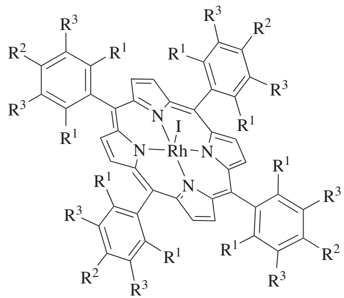


22 Cu(BOX7)

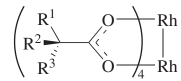


23 Cu(QOX)

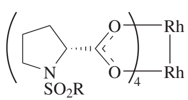
CHART 2. RHODIUM CATALYST COMPLEXES



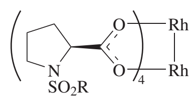
	R^1	R^2	R^3	
24:	H	H	H	RhTPPI
25:	Me	Me	H	RhTMPI
26:	Cl	H	H	RhTCPI



	R^1	R^2	R^3	
27:	R^1, R^2, R^3 = C_6F_5			$Rh_2(PFP)_4$
28:	Me	tetrachlorophthalimido	H	$Rh_2(TCPME)_4$
29:	Bn	tetrachlorophthalimido	H	$Rh_2(S\text{-}TCPTPA)_4$
30:	R^1, R^2, R^3 = triptycenyl			$Rh_2(TRIP)_4$
31:	Bn	phthalate	H	$Rh_2(S\text{-}PTPA)_4$
32:	R^1, R^2, R^3 = 4-$C_6F_{13}C_6H_4$			$Rh_2(PFHP)_4$
33:	R^1, R^2, R^3 = 3,5-$(C_8F_{17})_2C_6H_3$			$Rh_2(BFOP)_4$
34:	F	C_7F_{15}	F	$Rh_2(PFOC)_4$
35:	H	C_6F_{13}	H	$Rh_2(PFHM)_4$
36:	H	$CH_2C_6F_{13}$	H	$Rh_2(PFHE)_4$
37:	H	$CO(CH_2)_2C_{10}F_{21}$	H	$Rh_2(PFDE)_4$
38:	*t*-Bu	phthalate	H	$Rh_2(S\text{-}PTTL)_4$
39:	*t*-Bu	1,8-naphthalimidyl	H	$Rh_2(S\text{-}NTTL)_4$
40:	Ad	phthalate	H	$Rh_2(S\text{-}PTAD)_4$

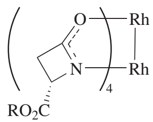


41 R = 4-$C_{12}H_{25}C_6H_4$ $Rh_2(R\text{-}DOSP)_4$

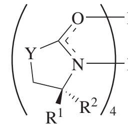


	R	
42:	4-$C_{12}H_{25}C_6H_4$	$Rh_2(S\text{-}DOSP)_4$
43:	4-*t*-BuC_6H_4	$Rh_2(S\text{-}TBSP)_4$
44:	C_8F_{17}	$Rh_2(FOSP)_4$

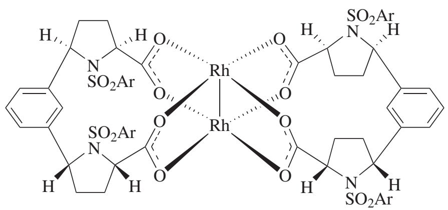
CHART 2. RHODIUM CATALYST COMPLEXES (*Continued*)



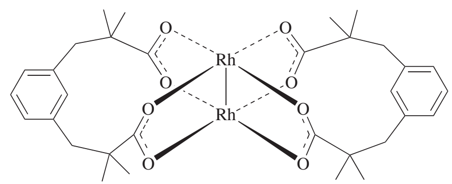
	R	
45:	*i*-Bu	$Rh_2(4S\text{-IBAZ})_4$
46:	Me	$Rh_2(S\text{-MEAZ})_4$
47:	L-menthyl	$Rh_2(S,S\text{-MenthAZ})_4$
48:	D-menthyl	$Rh_2(S,R\text{-MenthAZ})_4$



	Y	R^1	R^2	
49:	CH_2	H	CO_2Me	$Rh_2(5S\text{-MEPY})_4$
50:	CH_2	CO_2Me	H	$Rh_2(5R\text{-MEPY})_4$
51:	$NCO(CH_2)_2Ph$	H	CO_2Me	$Rh_2(4S\text{-MPPIM})_4$

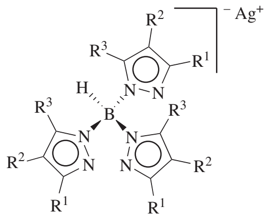


	Ar	
52:	$4\text{-}C_{12}H_{25}C_6H_4$	$Rh_2(S\text{-biDOSP})_2$
53:	$2,4,6\text{-}(i\text{-Pr})_3C_6H_2$	$Rh_2(S\text{-biTISP})_2$
54:	$4\text{-}t\text{-}BuC_6H_4$	$Rh_2(S\text{-biTBSP})_2$

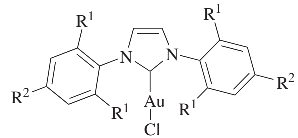


54a $Rh_2(esp)_2$

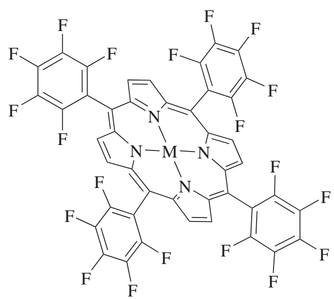
CHART 3. OTHER METAL CATALYST COMPLEXES



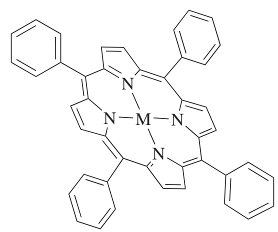
	R^1	R^2	R^3	
55:	CF_3	H	CF_3	$Tp^{(CF3)2}Ag$
56:	Br	Br	Br	$Tp^{Br3}Ag$



	R^1	R^2	
57:	*i*-Pr	H	Au(NHC1)
58:	Ad	H	Au(NHC2)
59:	*t*-Bu	H	Au(NHC3)
60:	Me	Me	Au(NHC4)

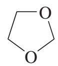
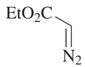
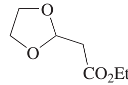
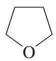
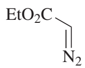
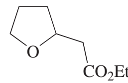
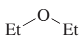
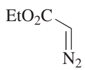
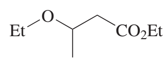
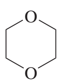
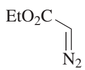
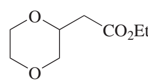


	M	
61:	Os	OsTPFPP
62:	FeCl	FeTPFPP

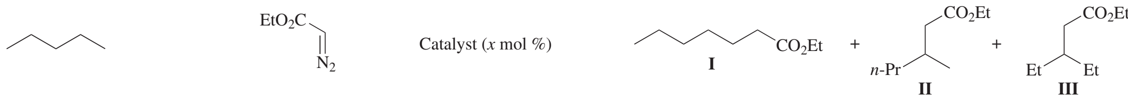


	M	
63:	Cu	CuTPP
64:	Ag	AgTPP
65:	FeCl	FeTPP

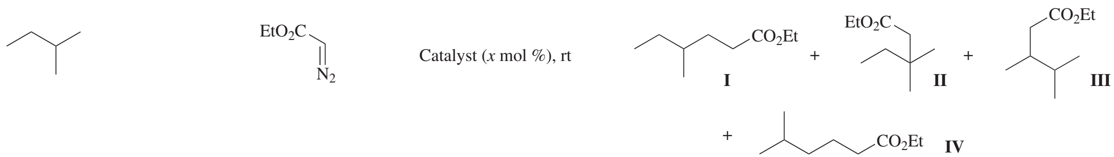
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Catalyst	x	Solvent	Time (h)	Yield (%)	Refs.
C_3 		Catalyst (x mol %), neat, rt, 2 h		$Tp^{Ms}Cu$ (**4**)	4.0			(95)	66
				$Tp^{Br3}Cu$ (**5**)	1.0			(>99)	67
C_4 		Catalyst (x mol %), rt		TpCu (**1**)	4.0	neat	4	(27)	66
				Tp*Cu (**2**)	4.0	neat	4	(39)	66
				$Tp^{Ms}Cu$ (**4**)	4.0	neat	2	(95)	66
				$Tp^{Ms}Cu$ (**4**)	4.0	neat	4	(98)	66
				$Tp^{Br3}Cu$ (**5**)	1.0	DCM	3	(>99)	67
				$Tp^{Cy}Cu$ (**6**)	4.0	neat	4	(72)	66
				$Tp^{Ph}Cu$ (**7**)	4.0	neat	4	(82)	66
				$Tp^{(CF3)2}Cu$ (**8**)	1.0	neat	15	(73)	64
				$Tp^{(CF3)2}Ag$ (**55**)	1.0	neat	15	(24)	64
		$Tp^{Br3}Cu$ (**5**) (1.0 mol %), neat, rt, 3 h						(>99)	67
		Catalyst (x mol%), neat, rt		$Tp^{Ms}Cu$ (**4**)	4.0		10	(20)	66
				$Tp^{Br3}Cu$ (**5**)	1.0		2	(20)	67

C_5

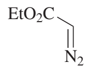
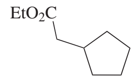


Catalyst	x	Solvent	Temp	Time (h)	**I + II + III**	**I:II:III**	
$Tp^{Br3}Cu$ (**5**)	5.0	DCM	rt	3	(50)	0:78:22	68
$Rh_2(TFA)_4$	0.1	neat	rt	4	(65)	7:66:27	61
$Rh_2(TFA)_4$	0.1	neat	35°	4	(92)	—	61
$Rh_2(OAc)_4$	1.0	neat	35°	4	(20)	4:63:33	62
$Rh_2(OPiv)_4$	1.0	neat	35°	4	(—)	5:64:33	62
$Rh_2(TFA)_4$	1.0	neat	rt	4	(65)	7:66:27	62
$Rh_2(PFP)_4$ (**27**)	1.0	neat	rt	4	(26)	7:62:31	62
Rh_2(S-TCPME)$_4$ (**28**)	1.0	neat	rt	4	(30)	12:64:24	62
Rh_2(S-TCPTPA)$_4$ (**29**)	1.0	neat	rt	4	(—)	16:61:23	62
$Rh_2(TRIP)_4$ (**30**)	1.0	neat	35°	4	(86)	30:61:9	62
$Tp^{(CF3)2}Ag$ (**55**)	1.0	neat	rt	15	(81)	0:81:19	64
$Tp^{Br3}Ag$ (**56**)	2.5	neat	rt	5	(93)	29:57:14	71
Au(NHC1) (**57**)	5.0	DCM	rt	13	(70)	26:55:19	133

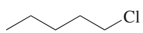
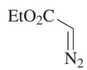
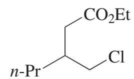
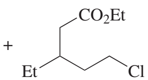
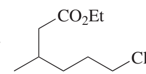
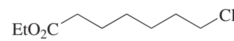


Catalyst	x	Solvent	Time (h)	**I + II + III + IV**	**I:II:III:IV**	
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	3	(53)	0:80:20:0	68
$Rh_2(TFA)_4$	0.1	neat	4	(71)	5:25:66:4	61
$Tp^{(CF3)2}Ag$ (**55**)	1.0	neat	15	(87)	0:35:65:0	64
$Tp^{Br3}Ag$ (**56**)	2.5	neat	5	(98)	21:21:36:20	71

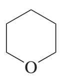
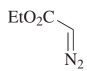
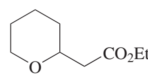
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 		Catalyst (x mol %), neat		

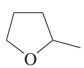
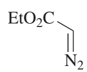
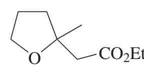
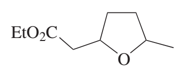
Catalyst	x	Temp	Time (h)		Refs.
$Rh_2(TFA)_4$	0.1	rt	4	(50)	61
$Rh_2(TFA)_4$	0.1	50°	4	(68)	61
$Tp^{Ms}Cu$ (**4**)	4.0	rt	20	(50)	66
$Tp^{(CF3)2}Cu$ (**8**)	1.0	rt	15	(60)	64
$Tp^{(CF3)2}Ag$ (**55**)	1.0	rt	15	(88)	64

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Catalyst (0.1 mol %), neat, 65°, 1.5 h	 **I** +  **II** +  **III** +  **IV**	60

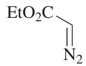
Catalyst	I + II + III + IV	I:II:III:IV
$Rh_2(OPiv)_4$	(<1)	1:15:74:10
RhTPPI (**24**)	(7)	4:17:69:10
RhTMPI (**25**)	(<1)	2:4:75:29
RhTCPI (**26**)	(13)	3:7:58:32

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Catalyst (x mol %), neat, rt		

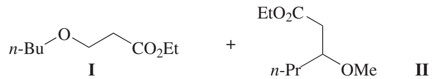
Catalyst	x	Time (h)		Refs.
$Tp^{Ms}Cu$ (**4**)	4.0	10	(84)	66
$Tp^{(CF3)2}Cu$ (**8**)	1.0	15	(75)	64
$Tp^{(CF3)2}Ag$ (**55**)	1.0	15	(41)	64

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Tp^{Br3}Cu$ (**5**) (1.0 mol %), DCM, rt, 3 h	 (30) +  (50)	67

n-BuOMe



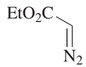
Catalyst (1.0 mol %),
DCM, rt, 3 h



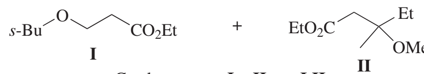
Catalyst	**I + II**	**I:II**
$Tp^{Ms}Cu$ (**4**)	(26)	41:59
$Tp^{Br3}Cu$ (**5**)	(70)	23:77
$Tp^{Cy}Cu$ (**6**)	(25)	9:91

67

s-BuOMe



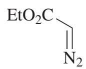
Catalyst (1.0 mol %),
DCM, rt, 3 h



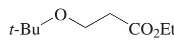
Catalyst	**I + II**	**I:II**
$Tp^{Ms}Cu$ (**4**)	(16)	77:23
$Tp^{Br3}Cu$ (**5**)	(50)	65:35
$Tp^{Cy}Cu$ (**6**)	(7)	21:79

67

t-BuOMe

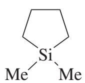
 5.0 eq

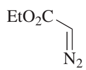
$Tp^{Br3}Cu$ (**5**) (1.0 mol %),
DCM, rt, 3 h

 (75)

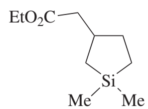
67

C_6



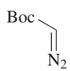
 *x* eq

$Rh_2(OAc)_4$ (2.0 mol %),
DCM, rt, 4 h

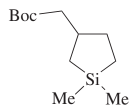


x	
1.5	(97)
1.7	(95)

74

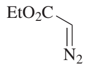
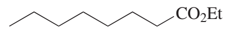
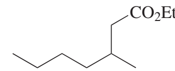
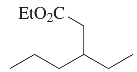
 3.0 eq

$Rh_2(OAc)_4$ (2.0 mol %),
DCM, rt, 4 h

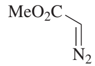
 (90)

74

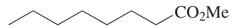
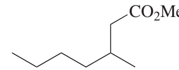
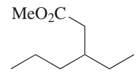
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Catalyst (*x* mol %)	 **I** +  **II** +  **III**	

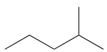
Catalyst	*x*	Solvent	Temp	Time (h)	**I** + **II** + **III**	**I**:**II**:**III**	Refs.
$Rh_2(OPiv)_4$	—	neat	60°	0.5	(50)	5:62:33	59
$Rh_2(OPiv)_4$	0.1	neat	65°	1.5	(50)	5:62:33	60
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	3	(45)	0:86:14	67
$Tp^{Br3}Cu$ (**5**)	5.0	DCM	rt	3	(71)	0:76:24	67
$Tp^{Cy}Cu$ (**6**)	5.0	DCM	rt	3	(12)	0:80:20	67
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	5	(50)	0:78:22	68
$Tp^{Ms}Cu(NCMe)$ (**12**)	5.0	DCM	rt	6	(24)	0:80:20	73
$Tp^{Ms}Cu(NCMe)$ (**12**)	5.0	$[bmim]PF_6$	rt	6	(21)	0:75:25	73
$Tp^{Ms*}Cu(NCMe)$ (**13**)	5.0	DCM	rt	6	(23)	0:75:25	73
$Tp^{Ms*}Cu(NCMe)$ (**13**)	5.0	$[bmim]PF_6$	rt	6	(21)	0:70:30	73
RhTPPI (**24**)	—	neat	60°	0.5	(46)	8:71:21	59
RhTPPI (**24**)	0.1	neat	65°	1.5	(46)	8:71:21	60
RhTMPI (**25**)	—	neat	60°	0.5	(36)	25:61:14	59
RhTMPI (**25**)	0.1	neat	65°	1.5	(36)	25:61:14	60
RhTCPI (**26**)	0.1	neat	65°	1.5	(36)	34:53:13	60
$Tp^{Br3}Ag$ (**56**)	2.5	neat	rt	5	(98)	23:56:21	71
Au(NHC1) (**57**)	5.0	DCM	rt	13	(78)	24:47:29	133

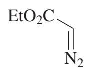


Catalyst (1.0 mol %), 40°, 8 h

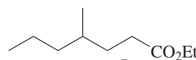
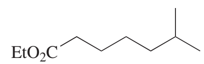
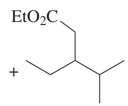
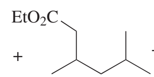

I
+

II
+

III

Catalyst	Solvent	**I + II + III**	**I:II:III**	
$Rh_2(OAc)_4$	PFMC	(4)	1:14:5.5	141
$Rh_2(PFHP)_4$ (**32**)	neat	(10)	1:24.8:9.4	134
$Rh_2(BFOP)_4$ (**33**)	PFMC	(64)	1:24.5:12.9	134
$Rh_2(PFOC)_4$ (**34**)	PFMC	(41)	1:15.6:7.4	141
$Rh_2(PFHM)_4$ (**35**)	PFMC	(39)	1:14.4:6.9	141
$Rh_2(PFHE)_4$ (**36**)	PFMC	(3)	—	141
$Rh_2(PFDE)_4$ (**37**)	PFMC	(4)	—	141





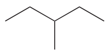
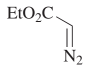
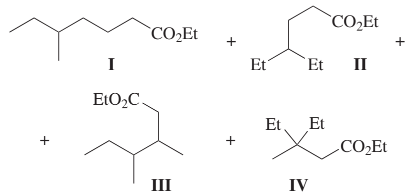
Catalyst (*x* mol %), rt


I
+

II
+

III
+

IV
+

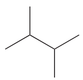
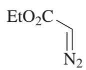
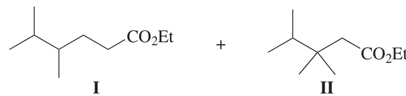
V

Catalyst	*x*	Solvent	Time (h)	**I + II + III + IV + V**	**I:II:III:IV:V**	
$Rh_2(TFA)_4$	0.1	neat	4	(68)	—	61
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	3	(44)	0:0:0:17:83	67
$Tp^{Br3}Cu$ (**5**)	5.0	DCM	3	(73)	0:0:0:23:77	67
$Tp^{Cy}Cu$ (**6**)	5.0	DCM	3	(9)	0:0:0:9:91	67
$Tp^{Ms}Cu(NCMe)$ (**12**)	5.0	DCM	3	(73)	0:0:0:38:62	68
$Tp^{Br3}Ag$ (**56**)	2.5	acetone	5	(92)	46[a]:0:36:19	71
Au(NHC1) (**57**)	5.0	DCM	13	(80)	30:18:41[b]:11	133

TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

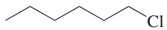
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Catalyst (x mol %), rt		

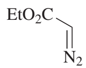
Catalyst	x	Solvent	Time (h)	**I + II + III + IV**	**I:II:III:IV**	Refs.
$Tp^{Br3}Ag$ (**56**)	2.5	neat	5	(98)	8:48:33:11	71
Au(NHC1) (**57**)	5.0	DCM	13	(65)	53:5:36:6	133

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Catalyst (x mol %), rt		

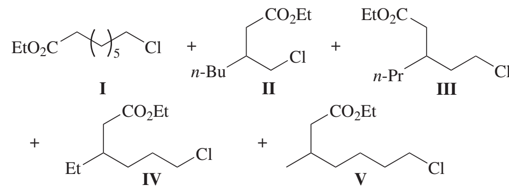
Catalyst	x	Solvent	Time (h)	**I + II**	**I:II**	Refs.
$Rh_2(TFA)_4$	0.1	neat	4	(46)	87:13	61
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	5	(30)	0:100	67
$Tp^{Br3}Cu$ (**5**)	5.0	DCM	5	(56)	0:100	67
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	5	(56)	0:100	68
$Tpm^{Ms}Cu(NCMe)$ (**12**)	5.0	DCM	6	(10)	0:100	73
$Tpm^{Ms}Cu(NCMe)$ (**12**)	5.0	$[bmim]PF_6$	6	(40)	0:100	73
$Tpm^{Ms*}Cu(NCMe)$ (**13**)	5.0	DCM	6	(13)	0:100	73
$Tpm^{Ms*}Cu(NCMe)$ (**13**)	5.0	$[bmim]PF_6$	6	(45)	0:100	73
Cu(NHC1) (**14**-$NaBAr'_4$)	5.0	DCM	13	$(48)^c$	10:90	133
Cu(NHC1) (**14**-NH_4PF_6)	5.0	DCM	13	$(99)^c$	3:97	133
Cu(NHC1) (**14**-$AgBF_4$)	5.0	DCM	13	$(74)^c$	0:100	133
Cu(NHC1) (**14**-AgOTf)	5.0	DCM	13	$(55)^c$	0:100	133

$Tp^{(CF3)2}Ag$ (**55**)	1.0	neat	15	(85)	0:100	64
$Tp^{Br3}Ag$ (**56**)	2.5	neat	5	(98)	60:40	71
Au(NHC1) (**57**)	5.0	DCM	13	(90)	83:17	133
Au(NHC2) (**58**)	5.0	DCM	13	(74)	60:40	133
Au(NHC3) (**59**)	5.0	DCM	13	(61)	53:47	133
Au(NHC4) (**60**)	5.0	DCM	13	(25)	32:68	133



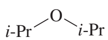


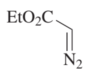
Catalyst (0.1 mol %), neat, 65°, 1.25 h



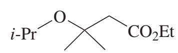
60

Catalyst	**I + II + III + IV + V**	**I:II:III:IV:V**
$Rh_2(OPiv)_4$	(2)	3:60:26:11:0
RhTPPI (**24**)	(38)	6:63:20:9:2
RhTMPI (**25**)	(8)	26:62:9:2:1

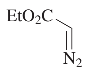




$Tp^{Br3}Cu$ (**5**) (1.0 mol %), DCM, rt, 3 h

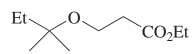


(47) 67



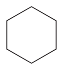
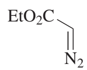
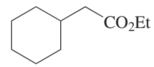
5.0 eq

$Tp^{Br3}Cu$ (**5**) (1.0 mol %), DCM, rt, 3 h



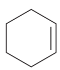
(25) 67

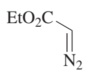
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		Catalyst (*x* mol %)		

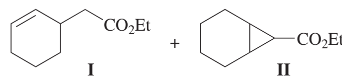
Catalyst	*x*	Solvent	Temp	Time (h)		Refs.
$CuSO_4$	100	neat	rt	1	(24)	58
CuCl	100	neat	rt	1	(15)	58
$[(bipy)_2Cu]$	0.2	DCM	rt	4	(10)	135
$[(bipy)_2Cu]$	0.2	DCM	rt	12	(18)	135
Tp*Cu (**2**)	4.0	DCM	rt	20	(3)	66
$Tp^{Np}Cu$ (**3**)	4.0	DCM	rt	20	(9.5)	66
$Tp^{Ms}Cu$ (**4**)	4.0	neat	rt	20	(54)	66
$Tp^{Ms}Cu$ (**4**)	4.0	DCM	rt	20	(29)	66
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	0.5	(5)	135
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	1	(12)	135
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	3	(13)	135
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	6	(16)	135
$Tp^{Ms}Cu$ (**4**)	5.0	DCM	rt	12	(27)	135
$Tp^{Cy}Cu$ (**6**)	4.0	DCM	rt	20	(19)	66
$Tp^{Ph}Cu$ (**7**)	4.0	DCM	rt	20	(20)	66
$Tp^{(CF3)2}Cu$ (**8**)	1.0	neat	rt	15	(58)	64
$Bp^{Br3}Cu$ (**9**)	0.5	DCM	rt	0.5	(8)	135
$Bp^{Br3}Cu$ (**9**)	0.5	DCM	rt	3	(13)	135
$Bp^{Br3}Cu$ (**9**)	0.2	DCM	rt	4	(36)	135
$Bp^{Br3}Cu$ (**9**)	0.2	DCM	rt	17	(49)	135
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	5	(90)	68
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	0.5	(16)	135
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	1	(77)	135

$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	3	(85)	135
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	6	(87)	135
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	rt	12	(87)	135
$Tpm^{Me2}Cu(NCMe)$ (**11**)	1.0	neat	rt	6	(30)	72
$Tpm^{Me2}Cu(NCMe)$ (**11**)	1.0	$[bmim]PF_6$	rt	6	(35)	72
$Tpm^{Ms}Cu(NCMe)$ (**12**)	5.0	DCM	rt	6	(77)	73
$Tpm^{Ms}Cu(NCMe)$ (**12**)	5.0	$[bmim]PF_6$	rt	6	(75)	73
$Tpm^{Ms*}Cu(NCMe)$ (**13**)	5.0	DCM	rt	6	(73)	73
$Tpm^{Ms*}Cu(NCMe)$ (**13**)	5.0	$[bmim]PF_6$	rt	6	(75)	73
Cu(NHC1) (**14**)	5.0	DCM	rt	13	(80)	133
$Rh_2(TFA)_4$	0.1	neat	rt	4	(78)	61
$Rh_2(TFA)_4$	0.1	neat	80°	4	(90)	61
$Rh_2(OPiv)_4$	—	neat	80°	5 min	(10)	75
$Rh_2(S\text{-DOSP})_4$ (**42**)	—	neat	80°	1.5	(34)	77
RhTPPI (**24**)	—	neat	60°	0.5	(71)	59
$Tp^{(CF3)2}Ag$ (**55**)	1.0	neat	rt	15	(88)	64
Au(NHC1) (**57**)	5.0	DCM	rt	13	(84)	133





Catalyst (2.0 mol %), 12 h



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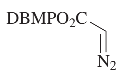
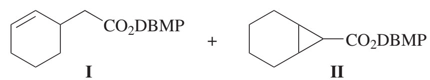
Catalyst	Solvent	Temp	**I + II**	**I:II**
$Cu(OMe)_3PI$	neat	83°	(8.5)	<5:95
$Rh_2(OAc)_4$	DCM	rt	(80)	20:80



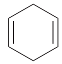
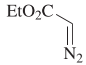
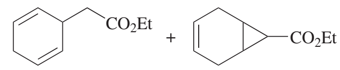
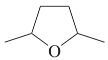
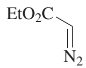
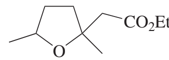
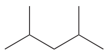
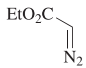
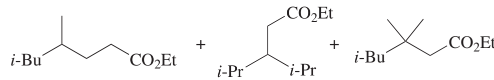
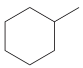
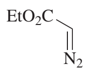
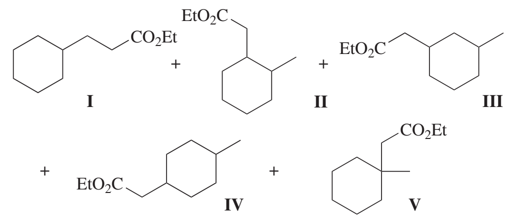
Catalyst (2.0 mol %),
DCM, rt, 12 h



76

Catalyst	**I + II**	**I:II**
$Rh_2(OAc)_4$	(54)	67:33
$Rh_2(pfb)_4$	(70)	33:67

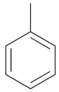
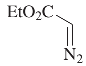
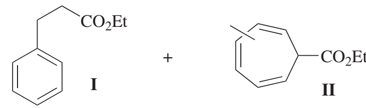
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			Catalyst (2.0 mol %), DCM, rt, 12 h	 I + II	76
				Catalyst / I + II / I:II: Cu (48) <5:95; $Rh_2(OAc)_4$ (90) <2:98	
			$Tp^{Br3}Cu$ (**5**) (1.0 mol %), DCM, rt, 3 h	 (41)	67
C_7			Catalyst (*x* mol %), rt	 I + II + III	
			Catalyst (*x* mol %), rt	 I + II + III + IV + V	

Catalyst	*x*	Solvent	Time (h)	**I** + **II** + **III**	**I**:**II**:**III**	Refs.
$Tp^{Br3}Ag$ (**56**)	2.5	neat	5	(98)	81:6:13	71
Au(NHC1) (**57**)	5.0	DCM	13	(65)	83:11:6	133

Catalyst	**I** + **II**	**I**:**II**
Cu	(48)	<5:95
$Rh_2(OAc)_4$	(90)	<2:98

Catalyst	*x*	Solvent	Time (h)	**I** + **II** + **III** + **IV** + **V**	**I**:**II**:**III**:**IV**:**V**	Refs.
$Tp^{Ms}Cu$ (**4**)	1.0	DCM	3	(60)	0:5[d]:76:19	67
$Tp^{Br3}Cu$ (**5**)	1.0	DCM	3	(97)	0:5[d]:65:30	67
$Tp^{Cy}Cu$ (**6**)	1.0	DCM	3	(10)	0:2[d]:39:59	67
$Rh_2(TFA)_4$	0.1	neat	4	(29)	—	61

C_7 		Catalyst (x mol %), neat		

Catalyst	x	Temp	Time (h)	**I + II**	**I**:**II**	
$Tp^{Ms}Cu$ (**4**)	1.0	rt	20	(20)	100:0	70
$Tp^{Br3}Cu(NCMe)$ (**10**)	1.0	rt	20	(68)	12:88	70
RhTPPI (**24**)	0.1	65°	1.25	(54)	9:91	60
RhTMPI (**25**)	0.1	65°	1.25	(42)	13:87	60

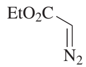
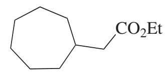
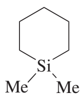
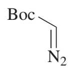
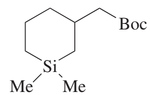
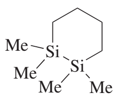
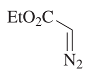
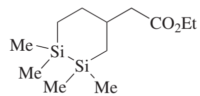
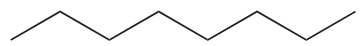
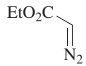
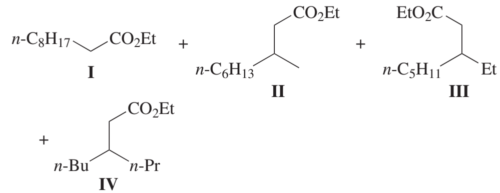
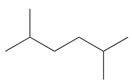
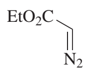
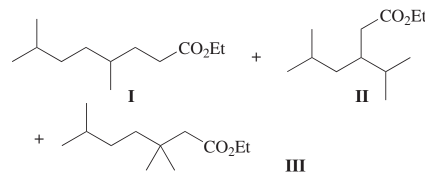
		$Rh_2(TFA)_4$ (0.1 mol %), neat, 4 h		Temp: rt (43); 119° (62)	61
		$Rh_2(OAc)_4$ (2.5 mol %), DCM, rt, 18 h		(63)	74
C_8 		$Rh_2(OAc)_4$ (1.9 mol %), DCM, rt, 4 h		(91)	74

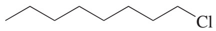
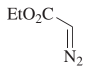
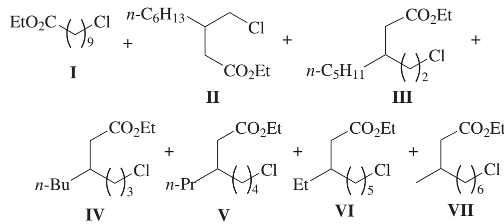
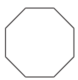
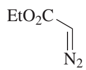
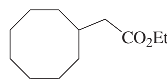
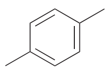
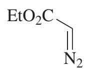
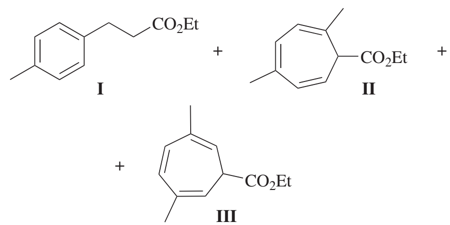
TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		Catalyst, neat		

Catalyst	Temp (°)	Time (h)	I + II + III + IV	I:II:III:IV	Refs.
$Rh_2(OPiv)_4$	60	0.5	(33)	3:49:27:21	59
$Rh_2(OPiv)_4$	65	1.5	(33)	3:49:27:21	60
RhTPPI (**24**)	60	0.5	(35)	6:52:22:20	59
RhTPPI (**24**)	65	1.5	(35)	6:52:22:20	60
RhTMPI (**25**)	60	0.5	(50)	21:52:14:13	59
RhTMPI (**25**)	65	1.5	(50)	19:56:14:11	60
RhTCPI (**26**)	65	1.5	(28)	29:47:13:11	60

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Catalyst (*x* mol %), rt		

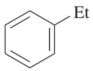
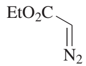
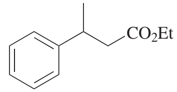
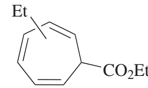
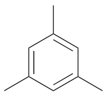
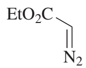
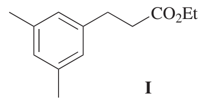
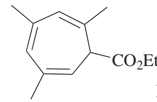
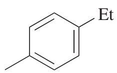
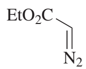
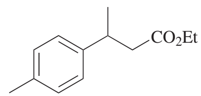
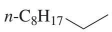
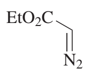
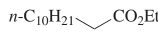
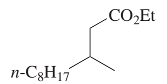
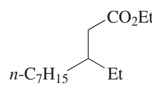
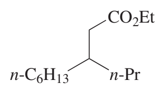
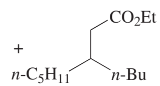
Catalyst	*x*	Solvent	Time (h)	I + II + III	I:II:III	Refs.
$Tp^{Br3}Cu(NCMe)$ (**10**)	5.0	DCM	3	(71)	0:0:100	68
$Tp^{Br3}Ag$ (**56**)	2.5	neat	5	(98)	45:17:36	71

Substrate	Diazo compound	Conditions	Product(s) and Yield(s) (%)	Refs.
		Catalyst, neat, 65°, 1.25 h		60
		$Rh_2(TFA)_4$ (0.1 mol %), neat, rt, 4 h	 (64)	61
		Catalyst, neat, 65°, 1.25 h		60

Catalyst	**I + II + III + IV + V + VI + VII**	**I:II:III:IV:V:VI:VII**
$Rh_2(OPiv)_4$	(9)	0:4:11:13:18:53:1
RhTPPI (**24**)	(71)	1:6:10:16:19:42:6
RhTMPI (**25**)	(12)	1:2:4:7:9:53:24

Catalyst	**I + II + III**	**I:II:III**
RhTPPI (**24**)	(62)	14:86:0
RhTMPI (**25**)	(33)	55:45:0
RhTCPI (**26**)	(50)	44:44:12

TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			Catalyst (1.0 mol %), neat, rt, 20 h	 **I** +  **II**	70
C_9			Catalyst (x mol %), neat	 **I** +  **II**	
			Catalyst (1.0 mol %), neat, rt, 20 h		70
C_{10}			Catalyst, neat	 **I** +  **II** +  **III** +  **IV** +  **V**	

C_8 entry:

Catalyst	**I + II**	**I:II**
$Tp^{Ms}Cu$ (**4**)	(56)	100:0
$Tp^{Br3}Cu(NCMe)$ (**10**)	(48)	63:37

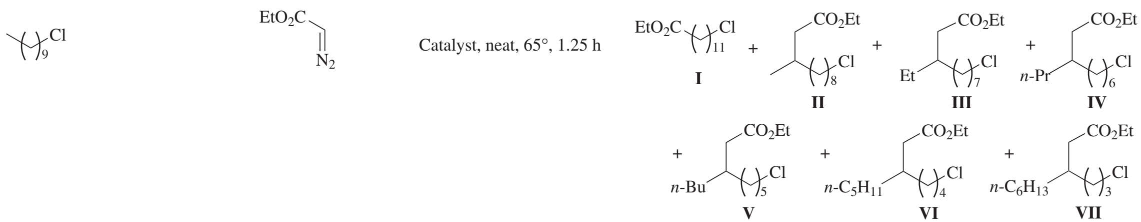
C_9 entry (mesitylene):

Catalyst	x	Temp	Time (h)	**I + II**	**I:II**	Refs.
$Tp^{Ms}Cu$ (**4**)	1.0	rt	20	(35)	86:14	70
$Tp^{Br3}Cu(NCMe)$ (**10**)	1.0	rt	20	(87)	14:86	70
RhTPPI (**24**)	—	65°	1.25	(74)	11:89	60
RhTMPI (**25**)	—	65°	1.25	(27)	78:22	60
RhTCPI (**26**)	—	65°	1.25	(61)	64:36	60

C_9 entry (4-ethyltoluene):

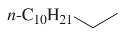
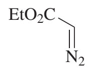
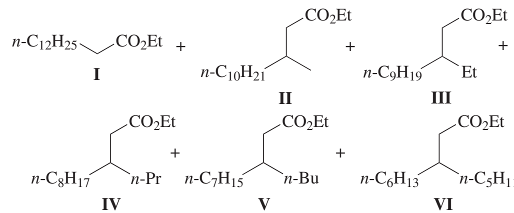
Catalyst	
$Tp^{Ms}Cu$ (**4**)	(58)
$Tp^{Br3}Cu(NCMe)$ (**10**)	(45)

Catalyst	Temp (°)	Time (h)	**I** + **II** + **III** + **IV** + **V**	**I**:**II**:**III**:**IV**:**V**	
$Rh_2(OPiv)_4$	60	0.5	(29)	2:42:20:18:18	59
$Rh_2(OPiv)_4$	65	1.5	(29)	2:42:20:18:18	60
RhTPPI (**24**)	60	0.5	(40)	5:40:19:18:18	59
RhTPPI (**24**)	65	1.5	(40)	5:40:19:18:18	60
RhTMPI (**25**)	60	0.5	(24)	20:48:11:10:11	59
RhTMPI (**25**)	65	1.5	(24)	17:52:11:10:10	60
RhTCPI (**26**)	65	1.5	(21)	28:42:11:10:9	60

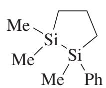
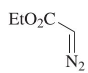
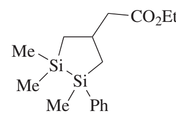
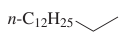
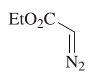
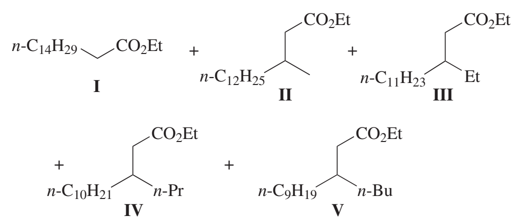


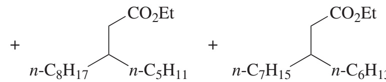
Catalyst	**I** + **II** + **III** + **IV** + **V** + **VI** + **VII**	**I**:**II**:**III**:**IV**:**V**:**VI**:**VII**	
$Rh_2(OPiv)_4$	(11)	1:41:16:13:9:16:4	60
RhTPPI (**24**)	(46)	3:37:13:12:11:19:5	
RhTMPI (**25**)	(15)	16:45:10:10:10:9:0	

TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 		Catalyst, neat		

Catalyst	Temp (°)	Time (h)	**I + II + III + IV + V + VI**	**I:II:III:IV:V:VI**	Refs.
$Rh_2(OPiv)_4$	60	0.5	(13)	1:32:17:15:18:17	59
$Rh_2(OPiv)_4$	65	1.5	(13)	1:32:17:15:18:17	60
RhTPPI (**24**)	60	0.5	(17)	4:33:20:13:15:15	59
RhTPPI (**24**)	65	1.5	(17)	4:33:20:13:15:15	60
RhTMPI (**25**)	60	0.5	(21)	20:45:10:9:8:8	59
RhTMPI (**25**)	65	1.5	(21)	15:47:10:10:10:8	60
RhTCPI (**26**)	65	1.5	(12)	26:38:10:9:10:7	60

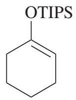
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		$Rh_2(OAc)_4$ (2.4 mol %), DCM, rt, 4 h	 (62)	74
C_{14} 		Catalyst, neat, 65°, 1.5 h		60

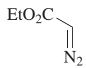


VI VII

Catalyst	**I + II + III + IV + V + VI + VII**	**I:II:III:IV:V:VI:VII**
$Rh_2(OPiv)_4$	(12)	1:32:14:13:13:14:13
RhTPPI (**24**)	(11)	3:30:14:12:13:15:13
RhTMPI (**25**)	(8)	14:43:10:8:9:8:8

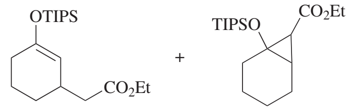
C_{15}





2.0 eq

Catalyst (2.0 mol %), DMB, –30°

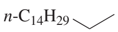


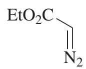
I **II**

Catalyst	**I + II**	**I:II**
$Rh_2(OOct)_4$	(66)	4:96
$Rh_2(S\text{-DOSP})_4$ (**42**)	(54)	24:76

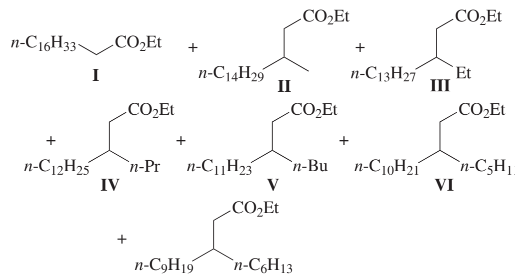
84

C_{16}





Catalyst, neat, 65°, 1.5 h

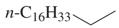
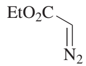
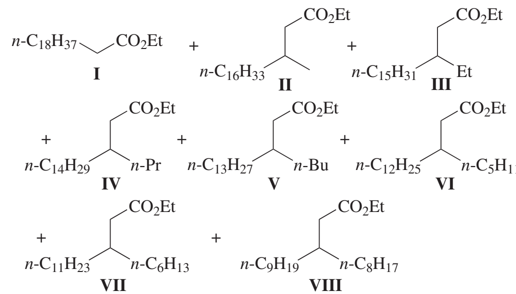
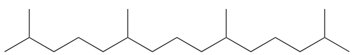
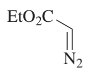
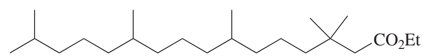
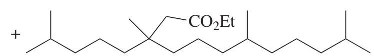


I **II** **III** **IV** **V** **VI** **VII**

60

Catalyst	**I + II + III + IV + V + VI + VII**	**I:II:III:IV:V:VI:VII**
$Rh_2(OPiv)_4$	(7)	2:32:13:11:12:9:21
RhTPPI (**24**)	(16)	3:25:12:13:12:13:22
RhTMPI (**25**)	(6)	14:39:9:8:8:8:14

TABLE 1. C–H INSERTION OF ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18} 		Catalyst, neat, 65°, 1.5 h		60
C_{19} 		$Tp^{Br3}Cu(NCMe)$ (**10**) (5.0 mol %), DCM, rt, 5 h	 (51) +  (34)	68

Catalyst	**I + II + III + IV + V + VI + VII + VIII**	**I**:**II**:**III**:**IV**:**V**:**VI**:**VII**:**VIII**
$Rh_2(OPiv)_4$	(11)	2:22:12:10:10:10:12:22
RhTPPI (**24**)	(27)	2:19:9:9:10:10:14:27
RhTMPI (**25**)	(7)	13:35:8:8:8:8:8:12

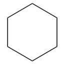
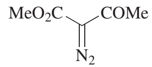
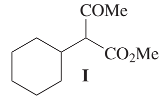
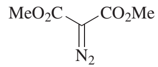
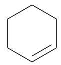
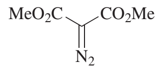
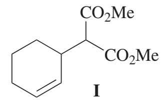
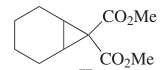
[a] The value is the combined yield of products **I** and **II**.

[b] The value is the combined yield of products **III** and **IV**.

[c] These values are percent conversions.

[d] The value is the combined yield of products **II** and **III**.

TABLE 2. C–H INSERTION OF ACCEPTOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS

	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			$Rh_2(OPiv)_4$ (2.0 mol %), neat, 81°	 **I** (65)	75
			Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, 81°	**I** (51) 3% ee	77
			Catalyst (2.0 mol %), 12 h	 **I** +  **II**	76

Catalyst	Solvent	Temp	**I + II**	**I:II**
$Cu(OMe)_3PI$	neat	83°	(63)	10:90
$Cu(acac)_2$	DCM	rt	(57)	9:91
$Rh_2(OAc)_4$	DCM	rt	(96)	38:62
$Rh_2(pfb)_4$	DCM	rt	(48)	52:48
Rh_2(*R*-BNP)$_4$	DCM	rt	(30)	49:51
Rh_2(*S*-PTPA)$_4$ (**31**)	DCM	rt	(86)	24:76

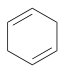
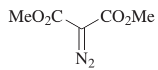
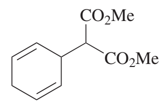
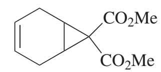
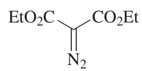
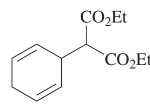
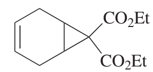
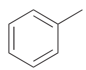
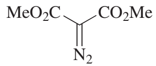
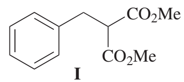
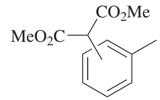
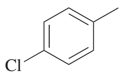
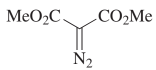
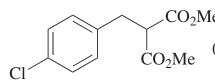
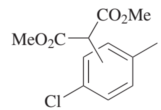
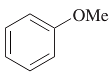
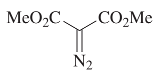
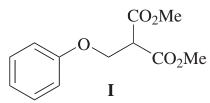
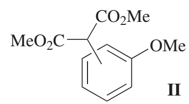
	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
			$Rh_2(OAc)_4$ (1.0 mol %), DCM, rt, 12 h	 (42) +  (21)	76
			CuCl (2.0 mol %), DCM, rt, 12 h	 (2) +  (26)	76

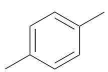
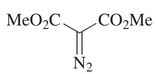
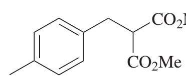
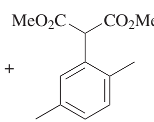
TABLE 2. C–H INSERTION OF ACCEPTOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM DIAZOESTERS (*Continued*)

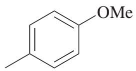
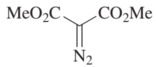
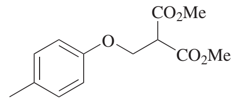
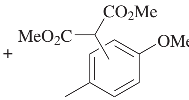
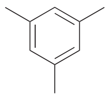
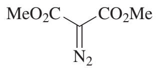
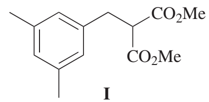
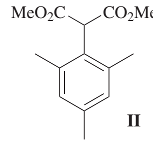
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		Catalyst (2.0 mol %), neat, 110°	 **I** +  **II**	65

Catalyst	Time (h)	**I + II**	**I:II**
FeTPFPP (**62**)	72	(51)	2:1
CuTPP (**63**)	54	(72)	2:1
AgTPP (**64**)	54	(74)	2:1
FeTPP (**65**)	54	(68)	2:1

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		FeTPP (**65**) (2.0 mol %), neat, 110°, 48 h	 (46) +  (5)	65
		Catalyst (2.0 mol %), neat, 110°, 16 h	 **I** +  **II**	65

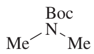
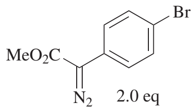
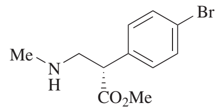
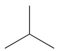
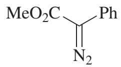
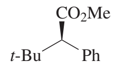
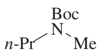
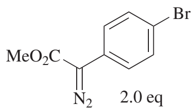
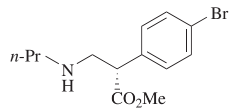
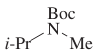
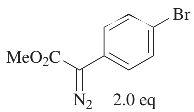
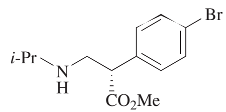
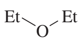
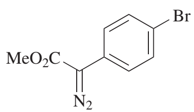
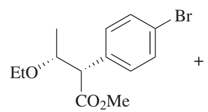
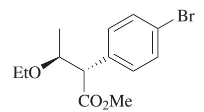
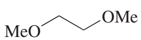
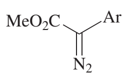
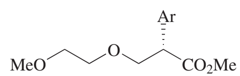
Catalyst	**I + II**	**I:II**
CuTPP (**63**)	(75)	5:1
AgTPP (**64**)	(78)	5:1
FeTPP (**65**)	(74)	5:1

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		FeTPP (**65**) (2.0 mol %), neat, 110°, 32 h	 (63) +  (13)	65

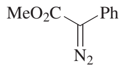
			FeTPP (**65**) (2.0 mol %), neat, 110°, 16 h	 (68) +  (8)	65
C_9			Catalyst (2.0 mol %), neat, 110°	 + 	65

Catalyst	Time (h)	**I** + **II**	**I**:**II**
FeTPFPP (**62**)	48	(56)	9:1
CuTPP (**63**)	32	(78)	9:1
AgTPP (**64**)	32	(79)	9:1
FeTPP (**65**)	32	(74)	9:1

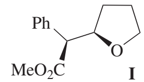
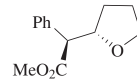
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. TFA, DCM, rt	 (61), 31% ee	88
C_4				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, –12°	 (20), 75% ee	53
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. TFA, DCM, rt	 (46), 64% ee	88
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. TFA, DCM, rt	 (57), 82% ee	88
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, rt, 2 h	 +  **I** + **II** (54), **I**:**II** = 3.2:1 76% ee **I**, 83% ee **II**	94
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, 2 h		94

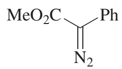
Ar	Temp		% ee
Ph	rt	(63)	75
4-BrC_6H_4	rt	(72)	76
4-MeC_6H_4	rt	(69)	67
4-$MeOC_6H_4$	70°	(56)	65
2-Np	rt	(72)	59



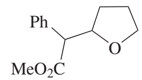
Rh_2(*S*-DOSP)$_4$ (**42**)
(1.0 mol %)


I
+

II

Solvent	Temp	Time (h)	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**	
neat	65°	2	(82)	2.3:1	60	61	77
neat	65°	11	(—)	—	72	—	53
neat	rt	11	(—)	—	84	—	53
neat	0˚	11	(—)	—	88	—	53
neat	–50°	11	(—)	—	90	—	53
hex	rt	11	(—)	—	92	—	53
hex	0˚	11	(—)	—	94	—	53
hex	–50°	11	(67)	2.7:1	97	18	53

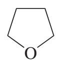
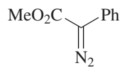
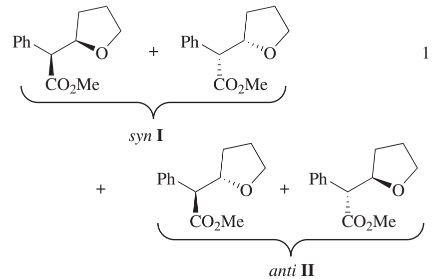


Catalyst (*x* mol %), neat

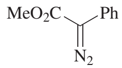


Catalyst	*x*	Temp (°)	Time (h)		
FeTPFPP (**62**)	100	65	24	(88)	136
FeTPP (**65**)	2.0	80	48	(48)	65

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

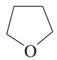
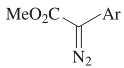
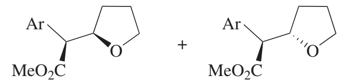
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		Catalyst (*x* mol %), 3 h		113

Catalyst	*x*	Solvent	Temp	*syn* **I** + *anti* **II** [a]	*syn* **I**/*anti* **II**	% ee *syn* **I**	% ee *anti* **II**
Cu(BOX1) (**16**)	2.0	neat	65°	(48)	1.8:1	59	40
Cu(BOX2) (**17**)	2.0	neat	65°	(49)	2.5:1	2	6
Cu(BOX7) (**22**)	2.0	neat	65°	(48)	2.4:1	14	27
Cu(BOX4) (**19**)	2.0	neat	65°	(85)	1.7:1	59	55
Cu(BOX4) (**19**)	4.0	neat	rt	(39)	1.4:1	57	40
Cu(BOX4) (**19**)	2.0	hex	65°	(20)	3:1	2	4
Cu(BOX5) (**20**)	2.0	neat	65°	(54)	2.9:1	1	12
Cu(BOX6) (**21**)	2.0	neat	65°	(75)	1.2:1	64	48
Cu(QOX) (**23**)	2.0	neat	65°	(44)	2.7:1	6	6

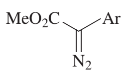
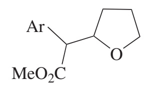


Immobilized catalyst (2.0 mol %), 65°, 2 h → *syn* **I** + *anti* **II** (113)

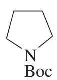
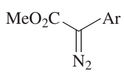
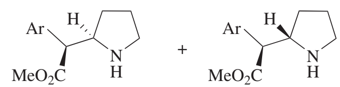
Catalyst	Solvent	Cycle	*syn* **I** + *anti* **II** [a]	*syn* **I**/*anti* **II**	% ee *syn* **I**	% ee *anti* **II**
Cu(BOX1) (**16**)	neat	1	(66)	3.1:1	84	39
Cu(BOX1) (**16**)	neat	2	(71)	3.4:1	83	40
Cu(BOX1) (**16**)	neat	3	(72)	3:1	82	39
Cu(BOX1) (**16**)	neat	4	(65)	2.6:1	81	40
Cu(BOX1) (**16**)	neat	5	(37)	1.2:1	28	24
Cu(BOX1) (**16**)	hex	1	(59)	3.5:1	88	46
Cu(BOX1) (**16**)	hex	2	(40)	3:1	85	46
Cu(BOX4) (**19**)	neat	1	(60)	2.8:1	58	51
Cu(BOX4) (**19**)	neat	2	(55)	2.9:1	57	51
Cu(BOX4) (**19**)	neat	3	(61)	2.8:1	56	54
Cu(BOX4) (**19**)	hex	1	(43)	2.6:1	71	56
Cu(BOX4) (**19**)	hex	2	(42)	2.5:1	66	53
Cu(BOX4) (**19**)	hex	3	(44)	2.4:1	66	56
Cu(BOX4) (**19**)	hex	1	(35)	1.7:1	44	9
Cu(BOX4) (**19**)	hex	2	(30)	1.7:1	45	8
Cu(BOX5) (**20**)	neat	1	(27)	1.1:1	2	16
Cu(BOX6) (**21**)	neat	1	(50)	1.5:1	62	59
Cu(BOX6) (**21**)	neat	2	(56)	1.3:1	61	59
Cu(BOX6) (**21**)	neat	3	(62)	1.3:1	58	56
Cu(QOX) (**23**)	neat	1	(31)	1.6:1	30	—
Cu(QOX) (**23**)	neat	2	(44)	1.4:1	41	2

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %)	 **I** + **II**	

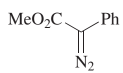
Ar	Solvent	Temp	Time (h)	**I + II**	**I**:**II**	% ee **I**	% ee **II**	Refs.
4-ClC_6H_4	hex	–50°	11	(74)	2.4:1	98	—	88
4-ClC_6H_4	neat	65°	2	(48)	1.7:1	52	51	77
4-ClC_6H_4	neat	rt	1	(57)	1.9:1	76	71	77
4-$O_2NC_6H_4$	neat	65°	2	(50)	1.8:1	69	58	77
4-MeC_6H_4	hex	–50°	11	(60)	4:1	97	—	88
4-$MeOC_6H_4$	hex	–50°	11	(56)	3.3:1	96	—	88
4-$MeOC_6H_4$	neat	65°	2	(63)	2.5:1	68	66	77
2-Np	hex	–50°	11	(62)	1.6:1	95	—	88

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		FeTPP (**65**) (2.0 mol %), neat, 80°		65

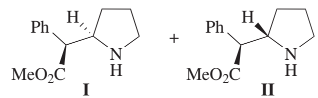
Ar	Time (h)	
4-ClC_6H_4	54	(52)
4-MeC_6H_4	48	(59)
4-$MeOC_6H_4$	32	(64)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		1. Catalyst (1.0 mol %), hex 2. DCM, TFA, rt, 1 h	 **I** + **II**	

Ar	Catalyst	Temp	Time (h)	**I + II**	**I**:**II**	% ee **I**	
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	–50°	13	(72)	96:4	94	80
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	rt	15	(75)	95:5	88	92
Ph	$Rh_2(OOct)_4$	69°	—	(49)	84:16	—	96
4-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	–50°	13	(70)	97:3	94	80
4-ClC_6H_4	$Rh_2(OOct)_4$	69°	—	(43)	79:21	—	96
4-BrC_6H_4	Rh_2(*R*,*S*-DOSP)$_4$	rt	—	(60)	97:3	—	96
4-IC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	–40° to rt	19	(41)	98:2	70	107
4-$TfOC_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	rt	19	(48)	98:2	85	107
4-MeC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	–50°	13	(67)	97:3	93	80
4-MeC_6H_4	$Rh_2(OOct)_4$	69°	—	(50)	93:7	—	96



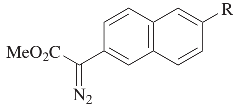
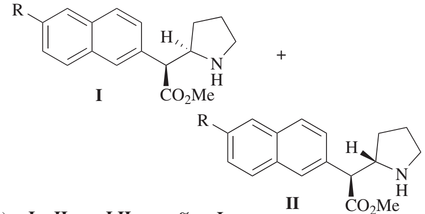
1. Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.6 mol %), toluene, rt, 18 h
2. DCM, TFA, rt, 4 h



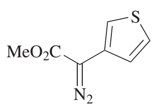
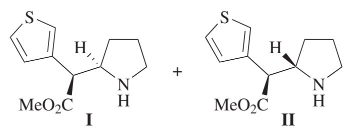
93

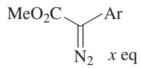
Cycle	**I + II**	**I**:**II**	% ee **I**
1	(70)	3:1	88
2	(67)	3:1	88
3	(68)	3:1	86

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

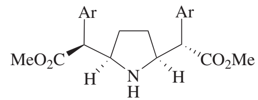
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		1. Catalyst (1.0 mol %), hex 2. DCM, TFA, rt		

R	Catalyst	Temp	Time (h)	**I** + **II**	**I**:**II**	% ee **I**	Refs.
H	Rh_2(*S*-DOSP)$_4$ (**42**)	–50°	13	(49)	96:4	93	80
H	Rh_2(*R*,*S*-DOSP)$_4$	rt	—	(43)	93:7	—	96
H	Rh_2(*S*-DOSP)$_4$ (**42**)	rt	—	(40)	93:7	75	96
H	Rh_2(*R*-DOSP)$_4$ (**41**)	rt	—	(40)	93:7	69 *ent*-**I**	96
Br	Rh_2(*R*,*S*-DOSP)$_4$	rt	—	(18)	89:11	—	96
Br	Rh_2(*R*-DOSP)$_4$ (**41**)	rt	—	(48)	90:10	85 *ent*-**I**	96
Me	Rh_2(*R*,*S*-DOSP)$_4$	rt	—	(22)	95:5	—	96
Me	Rh_2(*R*-DOSP)$_4$ (**41**)	rt	—	(32)	94:6	72 *ent*-**I**	96
OMe	Rh_2(*R*,*S*-DOSP)$_4$	rt	—	(21)	86:14	—	96
OMe	Rh_2(*R*-DOSP)$_4$ (**41**)	rt	—	(38)	89:11	75 *ent*-**I**	96

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt 2. DCM, TFA, rt	 **I** + **II** (64), **I**:**II** = 95:5 67% ee **I**	89

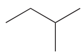


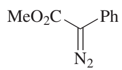
1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), 2,3-DMB, –50 to 58°, 15 h
2. DCM, TFA, rt, 4 h



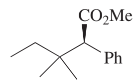
Ar	x		% ee	Refs.
Ph	6.0	(78)	97	80
Ph	2.0	(78)	97	92
4-ClC_6H_4	6.0	(50)	96	80
4-MeC_6H_4	6.0	(51)	96	80
4-$MeOC_6H_4$	6.0	(40)	97	80
2-Np	6.0	(62)	88	80

C_5



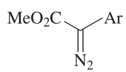


Catalyst (1.0 mol %), neat, rt, 1 h

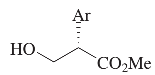


Catalyst		% ee
$Rh_2(OOct)_4$	(6)	—
$Rh_2(OPiv)_4$	(24)	—
$Rh_2(TFA)_4$	(19)	—
$Rh_2(TPA)_4$	(23)	—
Rh_2(*S*-DOSP)$_4$ (**42**)	(60)	68

53

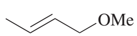


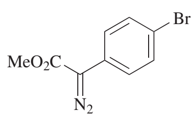
1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 2 h
2. DCM, $MeSO_3H$, rt, 0.5 h



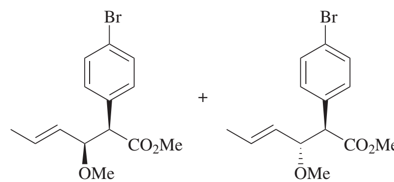
Ar		% ee
Ph	(34)	79
4-BrC_6H_4	(39)	85
4-MeC_6H_4	(21)	82
4-$MeOC_6H_4$	(36)	82
2-Np	(25)	76

94





Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 1 h



I + **II** (67), **I**:**II** = 2:1

56% ee **I**, 67% ee **II**

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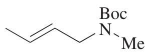
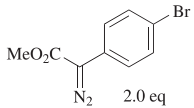
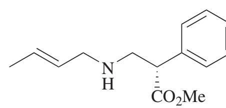
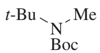
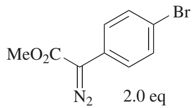
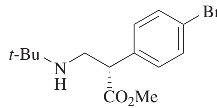
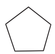
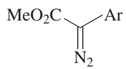
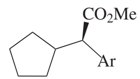
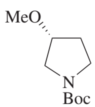
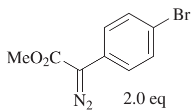
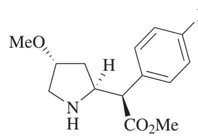
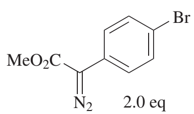
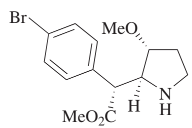
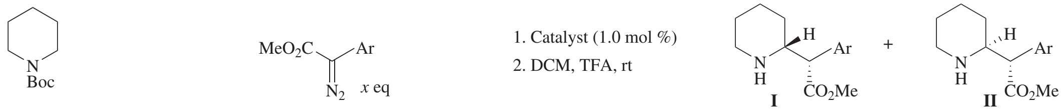
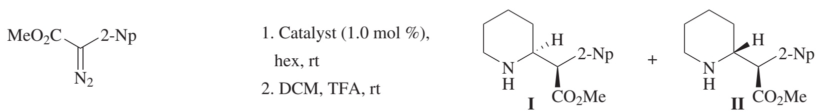
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5 	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt		(58), 85% ee	88
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt		(58), 54% ee	88
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat			
	 2.0 eq	1. Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, 50°, 5 h 2. DCM, TFA, rt, 14 h		(72), dr >97:3	92
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 5 h 2. DCM, TFA, rt, 14 h		(63), dr >97:3	92

Ar	Temp (°)	Time (h)		% ee	Refs.
Ph	50	1.5	(84)	87	77
Ph	10	2	(72)	96	53
4-ClC_6H_4	50	1.5	(78)	89	77
4-ClC_6H_4	10	2	(70)	95	53
4-$MeOC_6H_4$	50	1.5	(55)	83	77



Ar	x	Catalyst	Solvent	Temp	Time (h)	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**	
Ph	—	$Rh_2(OOct)_4$	hex	69°	—	(64)	1:2	—	—	96
Ph	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	2,3-DMB	rt	3.5	(49)	1.3:1	81	34	80
Ph	3.0	$Rh_2(S\text{-DOSP})_4$ (**42**)	2,3-DMB	rt	3.5	(86)	1:1	79	25	80
Ph	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	hex	–50°	—	(44)	1:1.8	89	68	96
Ph	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	hex	rt	15	(86)	1:1	79	25	92
Ph	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	hex	–50°	15	(44)	1:1.7	89	68	92
Ph	3.0	$Rh_2(S\text{-biDOSP})_2$ (**52**)	2,3-DMB	rt	3.5	(73)	1:2.4	65 *ent*-**I**	86 *ent*-**II**	80
Ph	—	$Rh_2(S\text{-biDOSP})_2$ (**52**)	hex	–50°	15	(52)	—	—	86 *ent*-**II**	92
4-ClC_6H_4	—	$Rh_2(OOct)_4$	hex	69°	—	(67)	1:1.4	—	—	96
4-ClC_6H_4	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	hex	–50°	—	(68)	1:1.5	94	77	96
3,4-$Cl_2C_6H_3$	—	$Rh_2(R,S\text{-DOSP})_4$	hex	rt	—	(28)	1:1.5	—	—	96
4-MeC_6H_4	—	$Rh_2(OOct)_4$	hex	69°	—	(55)	1:2	—	—	96
4-MeC_6H_4	—	$Rh_2(S\text{-DOSP})_4$ (**42**)	hex	–50°	—	(50)	1:1.4	92	57	96
4-PhC_6H_4	—	$Rh_2(OOct)_4$	hex	69°	—	(24)	1:1.6	—	—	96



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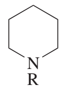
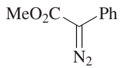
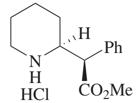
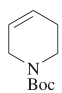
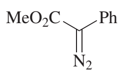
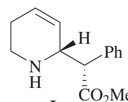
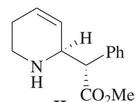
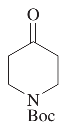
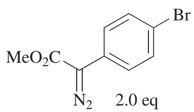
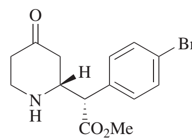
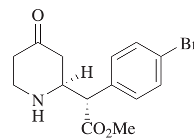
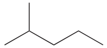
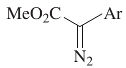
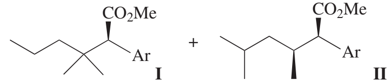
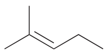
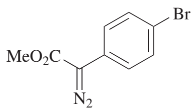
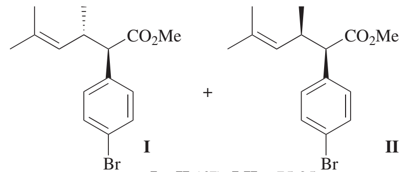
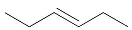
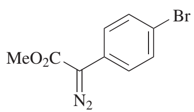
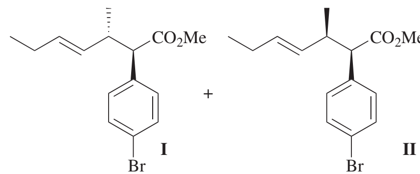
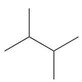
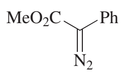
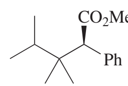
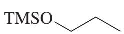
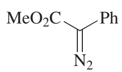
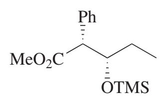
Catalyst	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
$Rh_2(R,S\text{-DOSP})_4$	(30)	1:2	—	—
$Rh_2(S\text{-biTISP})_2$ (**53**)	(33)	1:2	90	85

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 		1. Catalyst (1.0 mol %), cyclohexane, 4 h 2. MeOH, HCl, rt, 0.5 h		115
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), 2,3-DMB, rt, 3.5 h 2. DCM, TFA, rt, 2 h	 **I** +  **II** **I** + **II** (63), **I**:**II** = 4.6:1 80% ee **I**, 55% ee **II**	80, 92
	 2.0 eq	1. Catalyst (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt, 16 h	 **I** +  **II**	92

R	Catalyst	Temp (°)		% ee	dr
Alloc	Rh_2(5*R*-MEPY)$_4$ (**50**)	60	(—)	53	82:18
Boc	Cu(SALEN) (**15**)	–40	(—)	18	70:30
Boc	Rh_2(*S*-TBSP)$_4$ (**43**)	50	(—)	30	53:47
Boc	Rh_2(4*S*-IBAZ)$_4$ (**45**)	50	(44)	26	93:7
Boc	Rh_2(5*R*-MEPY)$_4$ (**50**)	50	(—)	69	97:3
Boc	Rh_2(4*R*-MPPIM)$_4$ (**51**)	90	(—)	16	55:45
Cbz	Rh_2(5*R*-MEPY)$_4$ (**50**)	80	(—)	45	82:18

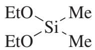
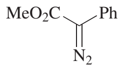
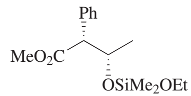
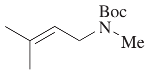
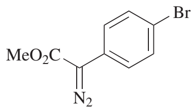
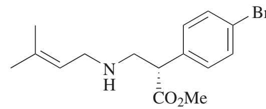
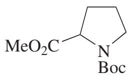
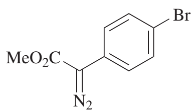
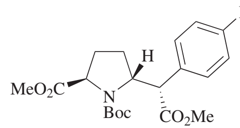
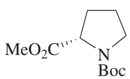
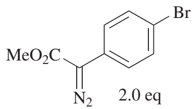
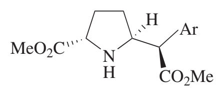
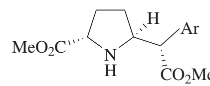
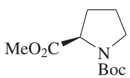
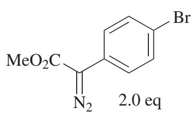
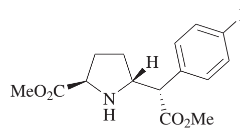
Catalyst	**I**	% ee **I**	**II**	% ee **II**
Rh_2(*S*-DOSP)$_4$ (**42**)	(31)	83	(20)	53
Rh_2(*S*-biTISP)$_2$ (**53**)	(46)	88 *ent*-**I**	(23)	76 *ent*-**II**

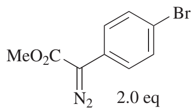
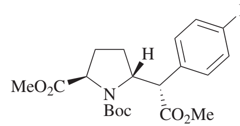
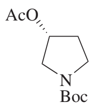
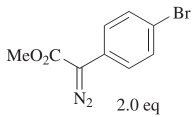
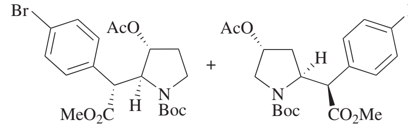
Substrate	Diazo compound	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, 62°, 2 h		53
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 **I** + **II** (67), **I**:**II** = 75:25, 86% ee **I** , 66% ee **II**	85
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 **I** + **II** (56), **I**:**II** = 56:44, 92% ee **I** , 80% ee **II**	85
		Rh_2(*S*-DOSP)$_4$ (**42**) (*x* mol %), neat, 58°		53
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol%), hex, rt, 3 h	 (47), 91% ee, dr >95:5	90

Ar	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**	dr **II**
Ph	75	58:42	26	86	80:20
4-BrC_6H_4	50	77:23	33	86	80:20

x		% ee
0.2	(4)	13
1.0	(24)	46
5.0	(27)	66

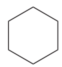
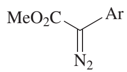
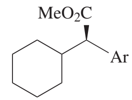
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), rt, 3 h	 (51), dr >95:5 Solvent / % ee DMB / 94 hex / 91	 82 90
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt	 (62), 87% ee	88
 *x* eq		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 94% ee, dr 93:7 *x* / % ee 2.0 (64) 77 4.0 (66) 79	86, 92
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 7 h 2. DCM, TFA, rt, 4 h	 (31) + Ar = 4-BrC_6H_4  (14)	86, 92
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h 2. DCM, TFA, rt, 4 h	 (68), dr >97:3	86

	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h		(83), dr >97:3	86, 92
	 2.0 eq	Catalyst (1.0 mol %), DMB, 50°, 4 h	 **I** + **II**		92

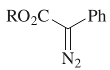
Catalyst	**I**	dr **I**	**II**	dr **II**
Rh_2(*S*-DOSP)$_4$ (**42**)	(41)	>97:3	(10)	75:25
Rh_2(*R*-DOSP)$_4$ (**41**)	—	—	(70)	>97:3

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

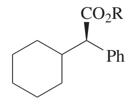
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Catalyst (*x* mol %)		

Ar	Catalyst	*x*	Solvent	Temp	Time (h)		% ee	Refs.
Ph	$Rh_2(OPiv)_4$	2.0	neat	81°	5 min	(94)	—	75
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	rt	5	(74)	92	137
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(80)	95	53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	rt	2	(80)	92	53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	39°	2	(81)	91	53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	50°	2	(69)	88	77, 53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	81°	2	(83)	81	77, 53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	0.1	neat	rt	2	(63)	91	53
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	0.01	neat	rt	2	(2)	70	53
Ph	$Rh_2(FOSP)_4$ (**44**)	1.0	neat	rt	5	(71)	61	137
Ph	$Rh_2(FOSP)_4$ (**44**)	1.0	neat	10°	5	(22)	61	137
Ph	$Rh_2(FOSP)_4$ (**44**)	1.0	PFMC	rt	5	(56)	61	137
Ph	$Rh_2(FOSP)_4$ (**44**) (immobilized)	1.0	neat	rt	5	(59)	58	137
Ph	FeTPP (**65**)	2.0	neat	81°	24	(66)	—	65
4-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(76)	94	53
4-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	81°	1.5	(91)	86	77
4-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	50°	1.5	(53)	93	77
4-ClC_6H_4	FeTPPI (**65**)	2.0	neat	81°	32	(58)	—	65
3-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(47)	94	53
2-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(81)	90	53

4-BrC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(64)	95	53
3-BrC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(62)	95	53
2-BrC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(72)	90	53
4-$CF_3C_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(78)	94	53
4-MeC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	10°	2	(63)	93	53
4-MeC_6H_4	FeTPP (**65**)	2.0	neat	81°	24	(72)	—	65
4-$MeOC_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	3.0	neat	10°	2	(23)	88	53
4-$MeOC_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	1.0	neat	50°	1.5	(85)	67	77
4-$MeOC_6H_4$	FeTPP (**65**)	2.0	neat	81°	16	(78)	—	65

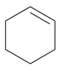


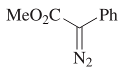
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, rt, 2 h



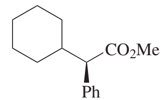
R		% ee
i-Pr	(39)	86
t-Bu	(45)	20

53

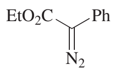




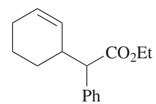
1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h
2. Pd/C, H_2, EtOH



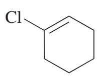
(58), 93% ee — 85

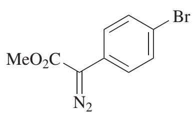


FeTPFPP (**62**) (1.0 eq), neat, 80°, 24 h

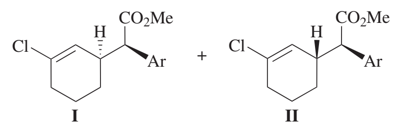


(64) — 136





Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, rt, 2 h



I + **II**

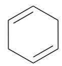
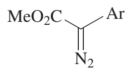
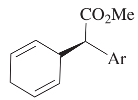
Ar = 4-BrC_6H_4

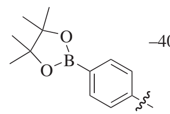
I + **II** (58), **I**:**II** = 66:34

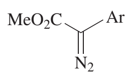
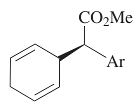
96% ee **I**, 10% ee **II**

85

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex		

Ar	Temp	Time (h)		% ee	Refs.
4-ClC_6H_4	rt	1	(84)	95	81
4-IC_6H_4	–40° to rt	3	(74)	95	107
3,4-$Cl_2C_6H_3$	–20°	—	(83)	93	87
4-MeC_6H_4	rt	1	(84)	94	81
4-$MeOC_6H_4$	rt	1	(69)	93	81
4-$TfOC_6H_4$	–40° to rt	3	(59)	94	107
	–40° to rt	3	(62)	89	107

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt		93

Ar	Cycle	Time (min)		% ee
Ph	1	20	(79)	88
Ph	3	20	(81)	87
Ph	5	23	(80)	87
Ph	8	25	(82)	84
Ph	10	30	(84)	84
4-ClC_6H_4	—	20	(82)	87
3,4-$Cl_2C_6H_3$	—	20	(81)	90
4-MeC_6H_4	—	20	(85)	85

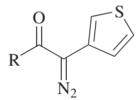
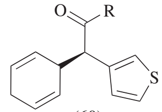
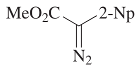
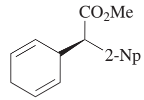
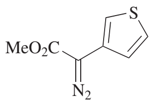
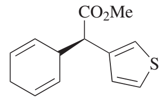
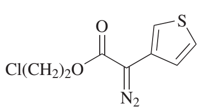
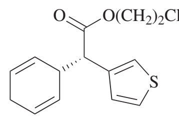
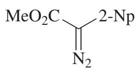
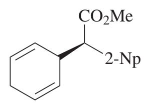
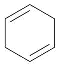
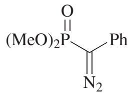
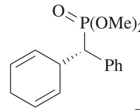
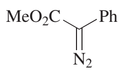
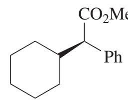
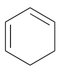
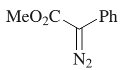
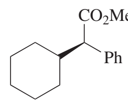
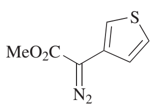
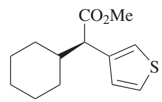
	Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt	 (60)	R / Time (min) / % ee OMe / 24 / 87 CH_2CH_2Cl / 20 / 86	93
	Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt, 23 min		(78), 82% ee	93
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), rt		Solvent / % ee hex (57) 88 DCM (55) 65	89
	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt		(55), 88% ee	89
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 1 h		(64), 92% ee	81

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		Catalyst (1.0 mol %), DMB, 50°, 5 h	 **I** Catalyst / % ee **I** Rh_2(*S*-PTTL)$_4$ (**38**) (67) 89 Rh_2(*S*-PTAD)$_4$ (**40**) (83) 92 Rh_2(*S*-DOSP)$_4$ (**42**) (62) 41 *ent*-**I** Rh_2(*S*-biTISP)$_2$ (**53**) (57) 72	111
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 1 h 2. Pd/C, H_2, EtOH	 (80), 91% ee	81
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 1 h 2. Pd/C, H_2, EtOH	 (48), 92% ee	81
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 1 h 2. Pd/C, H_2, EtOH	 (49), 70% ee	89

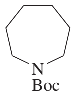
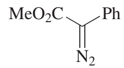
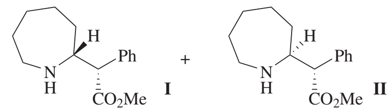
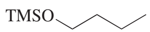
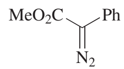
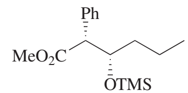
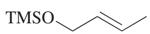
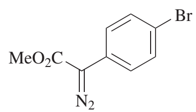
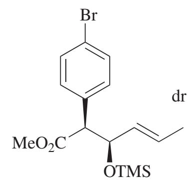
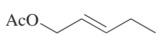
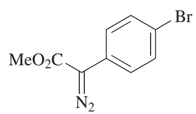
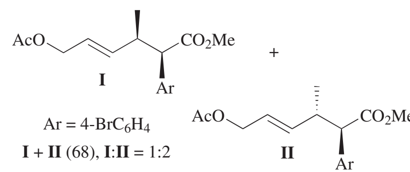
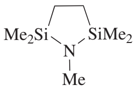
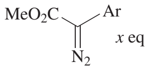
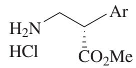
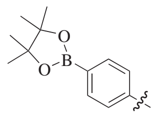
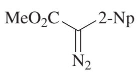
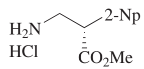
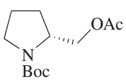
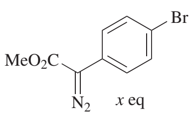
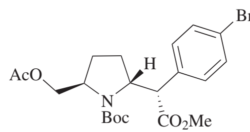
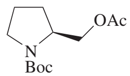
			1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 15 h 2. DCM, TFA, rt	 **I** + **II** (72), **I**:**II** = >95:5 92% ee **I**, —% ee **II**	92
C_7			Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (45), 87% ee, dr 95:5	90
			Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 1 h	 dr >97:3 <table><tr><th>Temp</th><th></th><th>% ee</th></tr><tr><td>rt</td><td>(89)</td><td>85</td></tr><tr><td>50°</td><td>(93)</td><td>65</td></tr></table>	90
			Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 Ar = 4-BrC_6H_4 **I** + **II** (68), **I**:**II** = 1:2 60% ee **I**, 76% ee **II**	90

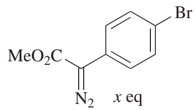
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 		1. Rh_2(*S*-DOSP)$_4$ (**42**) (*y* mol %), DMB 2. Et_2O, HCl, rt		105

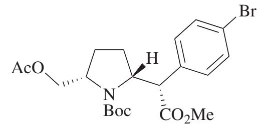
Ar	*x*	*y*	Temp	Time (h)		% ee
Ph	2.0	1.0	rt	2	(73)	84
Ph	2.0	1.0	–40°	2	(68)	93
Ph	0.5	2.0	–40°	2	(53)	97
4-BrC_6H_4	0.5	2.0	–40°	2	(53)	94
3,4-$Cl_2C_6H_3$	0.5	2.0	–40°	2	(30)	65
4-$MeOC_6H_4$	2.0	2.0	0°	5	(62)	93
4-$TfOC_6H_4$	2.0	2.0	0°	5	(63)	85
4-PhC_6H_4	0.5	2.0	–40°	2	(54)	95
	2.0	2.0	0°	5	(55)	71

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, 0°, 5 h 2. Et_2O, HCl, rt	 (75), 80% ee	105
	 *x* eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 dr >97:3 *x* = 1.0 (92) *x* = 2.0 (85)	92 86



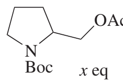


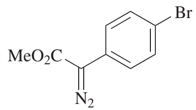
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h



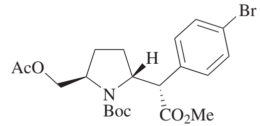
(20)

x	
1.0	92
2.0	86

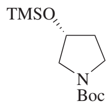


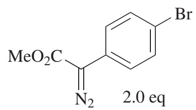


Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°

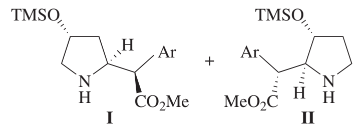


x	Time (h)		% ee	dr	
2.0	2	(58)	88	88:12	86
2.0	4	(62)	94	89:11	86, 92
4.0	4	(62)	94	89:11	92





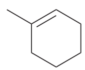
1. Catalyst (1.0 mol %), DMB, rt, 5 h
2. DCM, TFA, rt, 14 h

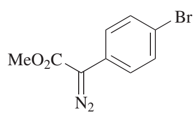


92

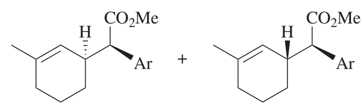
Ar = 4-BrC_6H_4

Catalyst	I	dr I	II	dr II
Rh_2(*R*-DOSP)$_4$ (**41**)	(73)	>97:3	(0)	—
Rh_2(*S*-DOSP)$_4$ (**42**)	(<5)	—	(50)	>97:3





Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, rt, 2 h

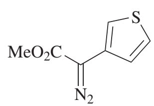


I Ar = 4-BrC_6H_4 **II**

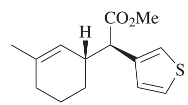
I + **II** (53), **I**:**II** = 17:83

94% ee **I**, 98% ee **II**

85



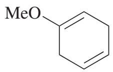
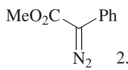
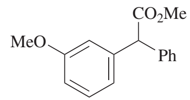
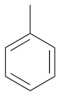
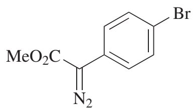
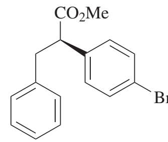
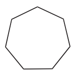
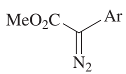
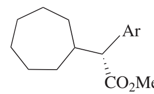
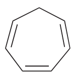
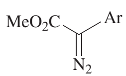
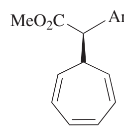
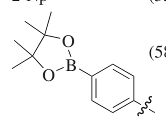
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt



(40), 94% ee, dr 75:25

89

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)			Refs.
C_7						
	 2.0 eq	1. $Rh_2(OAc)_4$ (1.0 mol %), DCM, 0°, 1 h 2. DDQ, benzene, rt, 3 h		(67)		138
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h		(6)		49
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, 118°, 1.5 h	 Ar		% ee	77
			Ph	(84)	70	
			4-ClC_6H_4	(96)	81	
			4-$MeOC_6H_4$	(78)	60	
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, –50°	 Ar		% ee	
			Ph	(55)	95	83
			4-ClC_6H_4	(64)	95	83
			4-IC_6H_4	(58)	91	107
			4-MeC_6H_4	(60)	94	83
			4-$TfOC_6H_4$	(52)	95	107
			2-Np	(53)	91	83
				(58)	88	107

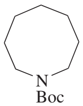
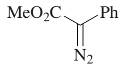
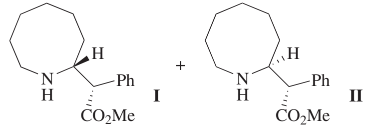
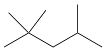
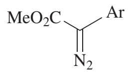
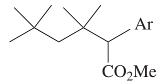
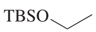
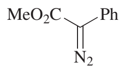
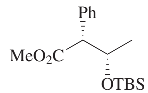
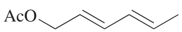
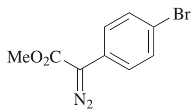
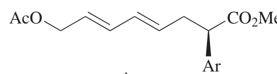
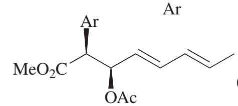
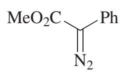
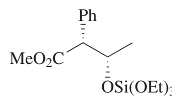
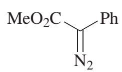
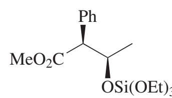
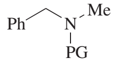
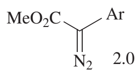
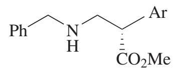
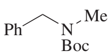
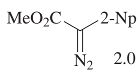
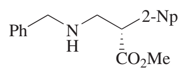
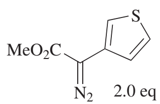
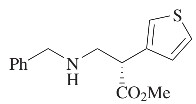
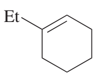
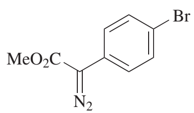
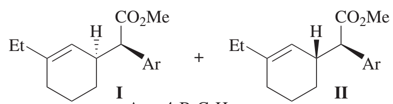
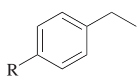
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 15 h 2. DCM, TFA, rt	 **I** + **II** (74), **I**:**II** = >95:5, 90% ee **I**, —% ee **II**	92
C_8				
		FeTPPI (**65**) (2.0 mol %), neat, 80°, 54 h	 Ar: 4-ClC_6H_4 (24); 4-MeC_6H_4 (31); 4-$MeOC_6H_4$ (37)	65
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (45), 96% ee, dr >95:5	90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (54), 84% ee +  (5), 70% ee, dr 93:7 Ar = 4-BrC_6H_4	90
$Si(OEt)_4$		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (70), 95% ee, dr >95:5	82, 90
		Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt	 (72), 96% ee, dr >95:5	93

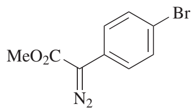
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt		88

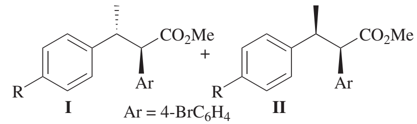
PG	Ar		% ee
Boc	4-BrC_6H_4	(62)	95
Boc	Ph	(67)	96
Boc	4-MeC_6H_4	(61)	92
Boc	4-$CF_3C_6H_4$	(55)	92
Boc	4-ClC_6H_4	(62)	96
Boc	2-$MeOC_6H_4$	(61)	92
Teoc	4-BrC_6H_4	(26)	94
Cbz	4-BrC_6H_4	(67)	90
Cbz	Ph	(77)	93
FMOC	4-BrC_6H_4	(21)	69

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt	 (55), 87% ee	88
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt	 (58), 90% ee	88
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 Ar = 4-BrC_6H_4 **I** + **II** (46), **I**:**II** = 25:75 90% ee **I**, 94% ee **II**	85



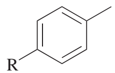


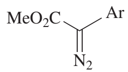
Rh$_2$(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h



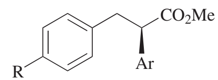
R	I + II	I:II	% ee I	% ee II
H	(49)	84:16	86	—
Br	(38)	73:27	88	58

49



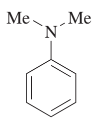


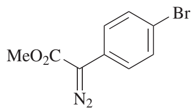
Rh$_2$(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 1 h



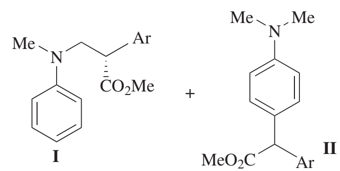
R	Ar	Temp		% ee
Me	4-BrC$_6$H$_4$	50°	(70)	74
OMe	Ph	0°	(14)	—
OMe	Ph	rt	(67)	79
OMe	Ph	50°	(67)	71
OMe	4-BrC$_6$H$_4$	0°	(69)	83
OMe	4-BrC$_6$H$_4$	rt	(73)	80
OMe	4-BrC$_6$H$_4$	50°	(71)	74
OMe	4-MeOC$_6$H$_4$	50°	(35)	67

91





Catalyst (1.0 mol %), rt, 1.5 h

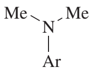
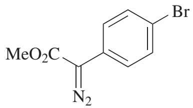
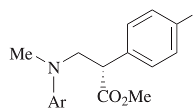
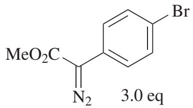
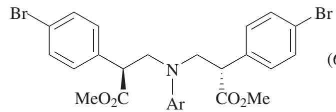
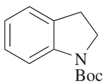
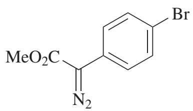
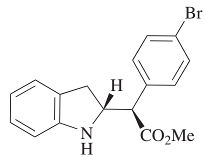
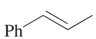
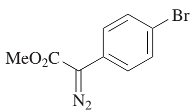
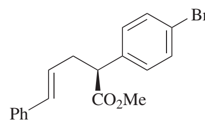
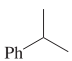
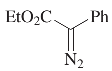
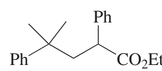


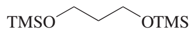
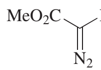
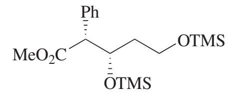
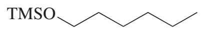
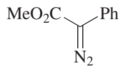
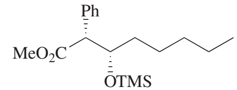
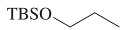
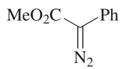
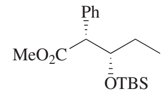
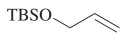
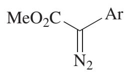
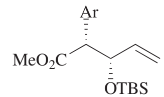
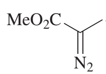
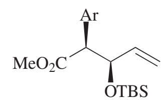
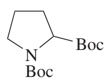
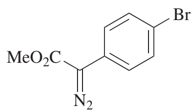
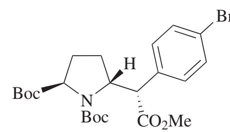
Catalyst	Solvent	I	II
Rh$_2$(OOct)$_4$	DMB	(15)	(9)
Rh$_2$(TFA)$_4$	DMB	(—)	(45)
Rh$_2$(*S*-DOSP)$_4$ (**42**)	DMB	(4)	(64)
Rh$_2$(*S*-DOSP)$_4$ (**42**)	DCM	(—)	(78)

Ar = 4-BrC$_6$H$_4$

98

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 Ar / % ee: 4-FC_6H_4 (70) 58; 4-BrC_6H_4 (72) 56	98
	 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (60) Ar / % ee: 4-FC_6H_4 89; 4-BrC_6H_4 90	98
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 5 h 2. DCM, TFA, rt, 4 h	 (38), 90% ee, dr >97:3	92
C_9 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 5 h	 (51), 84% ee	109
		FeTPFPP (**62**) (1 eq), neat	 Temp / Time (h): rt 48 (15); 60° 24 (67); 80° 15 (83)	136

	 x eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h		81
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (59), 86% ee, dr 95:5	90
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (36), 93% ee, dr >95:5	90
		Catalyst (1.0 mol %), hex, rt, 2 h		79
	 x eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol%), DMB, 1 h		90
 x eq		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol%), DMB, 50°, 4 h	 dr >97:3	86, 92

Row 1 product data:

x		% ee	dr
0.5	(44)	79	94:6
2.0	(71)	71	92:8

Row 4 product data:

Ar	Catalyst		% ee	dr
Ph	Rh_2(*R*-DOSP)$_4$ (**41**)	(52)	92	>97:3
4-ClC_6H_4	Rh_2(R,S-DOSP)$_4$	(35)	—	99:1
4-ClC_6H_4	Rh_2(*R*-DOSP)$_4$ (**41**)	(35)	90	99:1

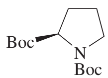
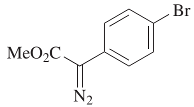
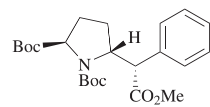
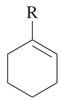
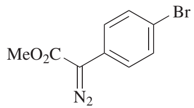
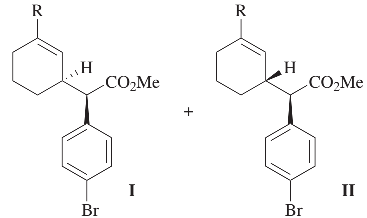
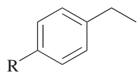
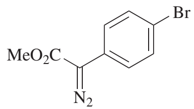
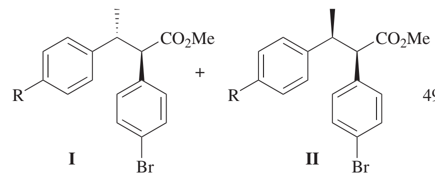
Row 5 product data:

Ar	*x*	Temp		% ee	dr
Ph	0.5	rt	(52)	92	>97:3
4-ClC_6H_4	0.5	rt	(36)	90	99:1
4-BrC_6H_4	2.0	50°	(33)	85	>97:3

Row 6 product data:

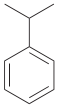
x		% ee
2.0	(58)	83
4.0	(60)	87

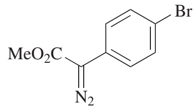
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 (85), dr >97:3	86
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h		85
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h		49

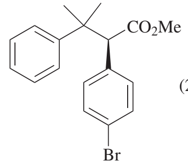
R	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
TMS	(48)	70:30	88	—
i-Pr	(65)	36:64	90	93

R	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
Me	(64)	82:18	89	74
OMe	(86)	68:32	89	76



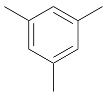


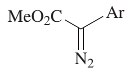
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h



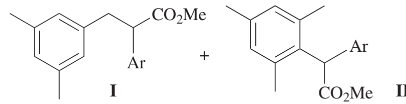
(23)

49



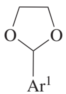


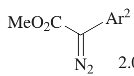
Catalyst (2.0 mol %), neat, 80°



65

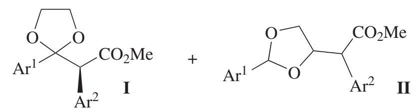
Ar	Catalyst	Time (h)	**I** + **II**	**I**:**II**
Ph	FeTPFPP (**62**)	16	(79)	1.0:0.7
Ph	FeTPP (**65**)	16	(82)	1.0:1.5
4-ClC_6H_4	FeTPFPP (**62**)	16	(72)	1.0:1.3
4-ClC_6H_4	FeTPP (**65**)	24	(78)	1.0:0.9
4-MeC_6H_4	FeTPFPP (**62**)	16	(79)	1.0:0.4
4-MeC_6H_4	FeTPP (**65**)	16	(84)	1.0:2.3
4-$MeOC_6H_4$	FeTPFPP (**62**)	16	(72)	1.0:0.3
4-$MeOC_6H_4$	FeTPP (**65**)	12	(86)	1.0:0.7





2.0 eq

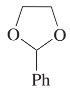
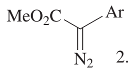
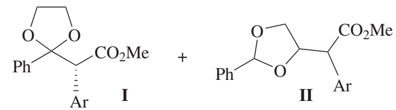
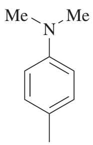
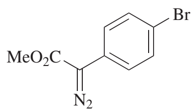
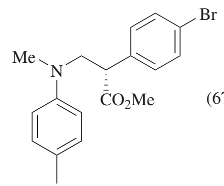
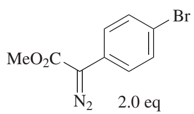
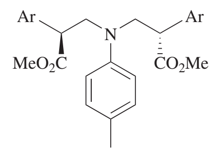
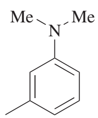
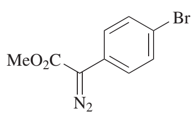
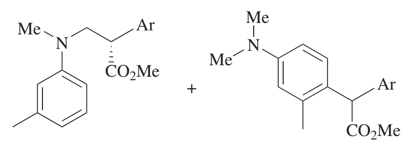
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %)



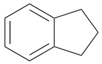
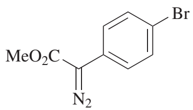
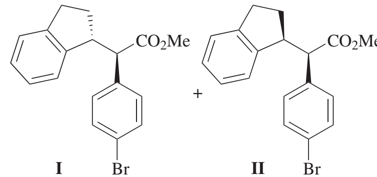
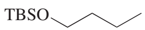
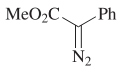
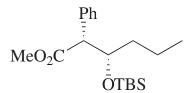
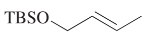
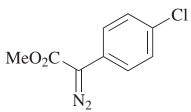
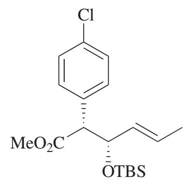
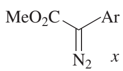
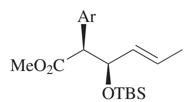
101

Ar^1	Ar^2	Solvent	Temp	Time (h)	**I** + **II**	**I**:**II**	% ee **I**	dr **II**
Ph	Ph	DMB	–15°	3	(80)	80:20	—	75:25
Ph	Ph	DMB	rt	3	(88)	66:34	—	68:32
Ph	Ph	DMB	50°	3	(76)	71:29	—	65:35
Ph	4-BrC_6H_4	DMB	rt	3	(75)	89:11	—	67:33
4-BrC_6H_4	4-BrC_6H_4	TFT	–15°	15	(70)	—	68	—

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

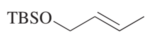
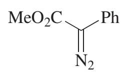
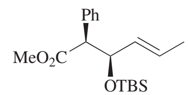
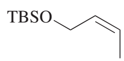
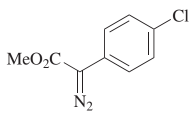
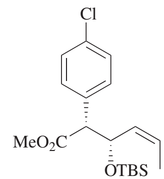
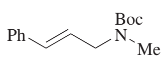
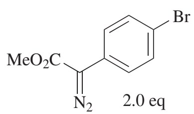
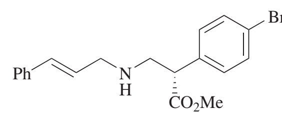
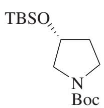
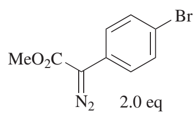
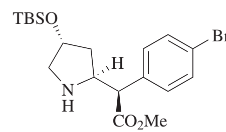
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	 2.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, –15°, 3 h	 Ar | **I** + **II** | **I**:**II** | dr **II** Ph | (41) | 83:17 | 78:22 4-BrC_6H_4 | (79) | 94:6 | 77:23	101
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (67), 53% ee	98
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (41), 91% ee Ar = 4-BrC_6H_4	98
		Catalyst (1.0 mol %), DMB, rt, 1.5 h	 **I** Ar = 4-BrC_6H_4 **II** Catalyst | **I** | % ee **I** | **II** $Rh_2(OOct)_4$ | (24) | — | (6) Rh_2(*S*-DOSP)$_4$ (**42**) | (24) | 64 | (36)	98

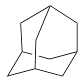
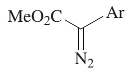
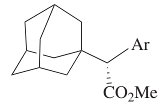
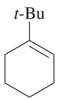
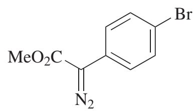
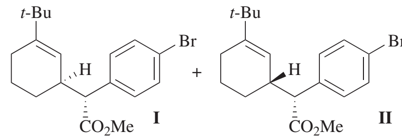
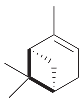
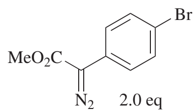
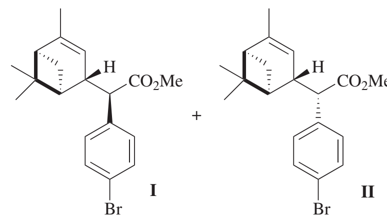
C$_{10}$

		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h	 **I** + **II** (62), **I**:**II** = 80:20; 89% ee **I**, 85% ee **II**	49
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (24), 81% ee, dr 94:6	90
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 2 h	 (72), 80% ee, dr 98:2	79
	 *x* eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, 2 h		90

Ar	*x*	Temp		% ee	dr
4-BrC_6H_4	2.0	rt	(65)	79	>97:3
4-BrC_6H_4	2.0	50°	(71)	68	>97:3
4-ClC_6H_4	0.5	rt	(72)	80	98:2

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

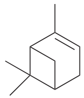
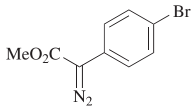
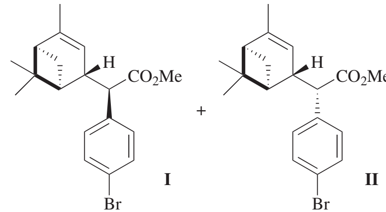
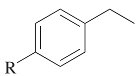
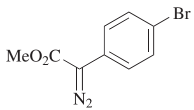
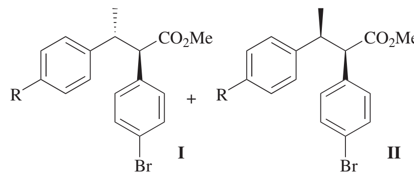
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt	 82% ee, dr >97:3; Cycle 1 (70), 2 (68), 3 (68)	93
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 2 h	 (72), dr 98:2	79
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. TFA, DCM, rt	 (60), 87% ee	88
	 2.0 eq	1. Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 5 h 2. TFA, DCM, rt, 14 h	 (71), dr >97:3	92

Substrate	Carbenoid precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h		53
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 **I** + **II** (46), **I**:**II** = 62:38 91% ee **I**, 81% ee **II**	85
	 2.0 eq	Catalyst (1.0 mol %), DMB, rt, 3 h		85

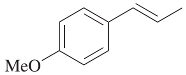
Ar		% ee
Ph	(67)	90
4-BrC_6H_4	(70)	96

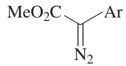
Catalyst	**I** + **II**	**I**:**II**
Rh_2(*S*-DOSP)$_4$ (**42**)	(93)	98:2
Rh_2(*R*-DOSP)$_4$ (**41**)	(62)	24:76

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

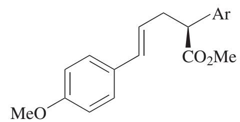
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 **I** + **II** **I** + **II** (52), **I**:**II** = 88:12; 99% ee **I**, —% ee **II**	85
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h	 **I** + **II**	49

R	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
Et	(71)	75:25	89	70
OAc	(77)	78:22	86	53
CO_2Me	(56)	80:20	83	58



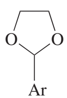


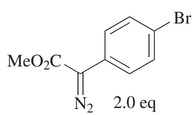
Catalyst (1.0 mol %),
DMB, rt, 5 h



Ar	Catalyst		% ee
Ph	$Rh_2(TPA)_4$	(88)	—
Ph	$Rh_2(esp)_2$ (**54a**)	(22)	—
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	(53)	91
4-BrC_6H_4	$Rh_2(OAc)_4$	(19)	—
4-BrC_6H_4	$Rh_2(OPiv)_4$	(10)	—
4-BrC_6H_4	$Rh_2(TFA)_4$	(18)	—
4-BrC_6H_4	$Rh_2(TPA)_4$	(74)	—
4-BrC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	(62)	93
4-ClC_6H_4	$Rh_2(TPA)_4$	(74)	—
4-ClC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	(46)	92
4-$CF_3C_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	(37)	80
4-MeC_6H_4	Rh_2(*S*-DOSP)$_4$ (**42**)	(58)	92
4-$MeOC_6H_4$	$Rh_2(TPA)_4$	(74)	—
4-$MeOC_6H_4$	$Rh_2(esp)_2$ (**54a**)	(27)	—
4-$MeOC_6H_4$	Rh_2(*S*-DOSP)$_4$ (**42**)	(67)	79

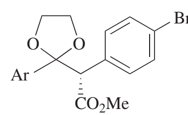
109





2.0 eq

Rh_2(*R*-DOSP)$_4$ (**41**)
(1.0 mol %),
TFT, –15°, 15 h



Ar		% ee
4-MeC_6H_4	(61)	70
4-$MeOC_6H_4$	(25)	74

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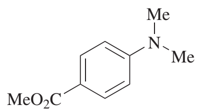
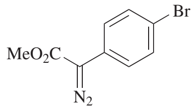
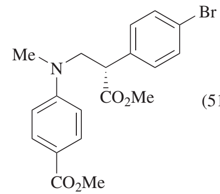
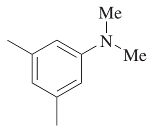
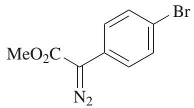
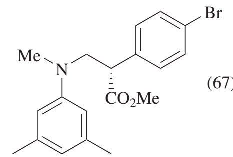
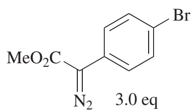
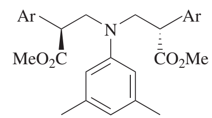
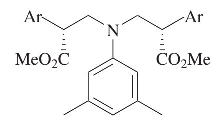
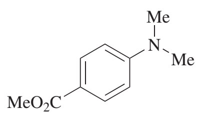
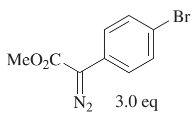
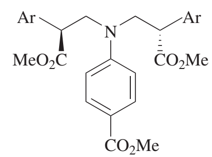
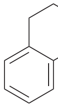
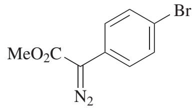
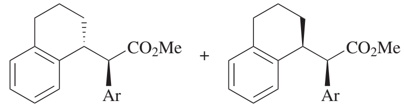
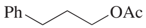
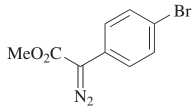
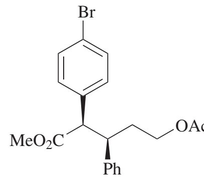
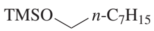
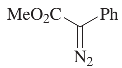
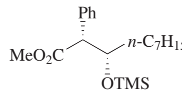
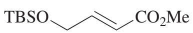
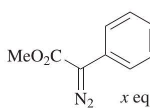
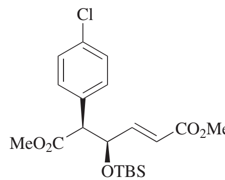
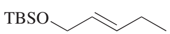
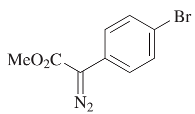
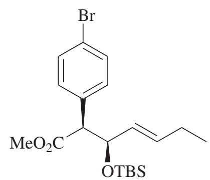
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

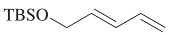
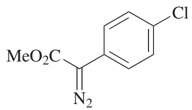
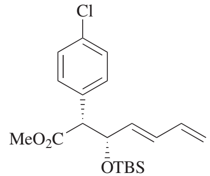
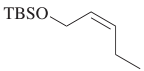
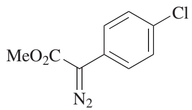
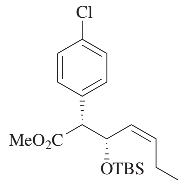
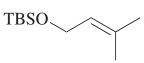
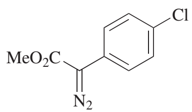
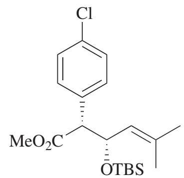
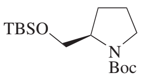
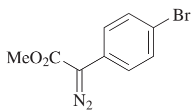
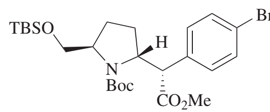
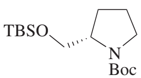
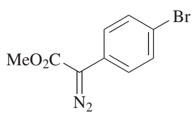
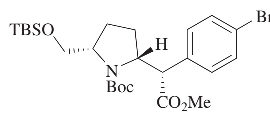
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (51), 71% ee	98
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (67), 74% ee	98
	 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, rt, 1.5 h	 (57), 95% ee Ar = 4-BrC_6H_4 +  (19)	98
	 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h	 (54), 85% ee Ar = 4-BrC_6H_4	98

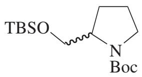
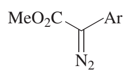
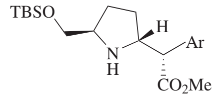
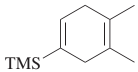
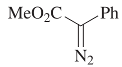
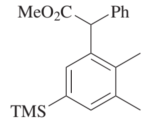
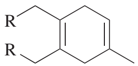
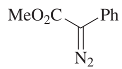
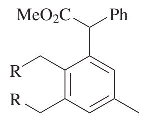
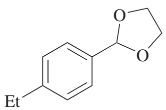
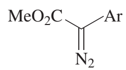
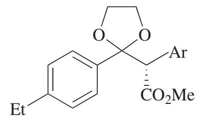
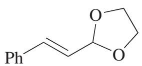
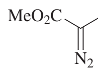
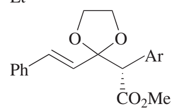
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h	 **I** Ar = 4-BrC_6H_4 **II** **I** + **II** (43), **I**:**II** = 42:58 67% ee **I**, 89% ee **II**	49
C_{11}				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (23), 62% ee, dr 80:20	90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 3 h	 (40), 84% ee, dr 95:5	90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 1 h		90

x		% ee	dr
0.5	(34)	51	>97:3
1.0	(93)	48	>97:3

Temp		% ee	dr
rt	(40)	78	>97:3
50°	(94)	62	>97:3

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

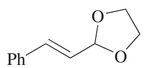
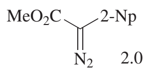
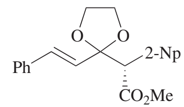
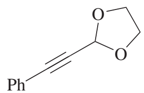
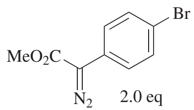
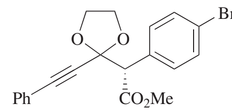
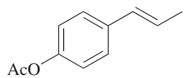
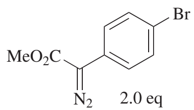
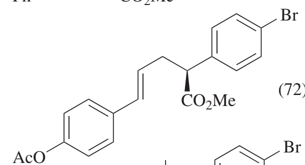
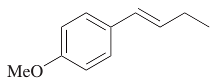
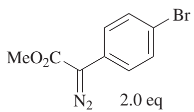
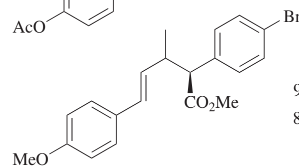
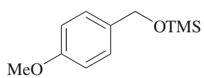
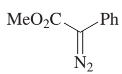
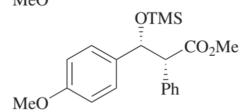
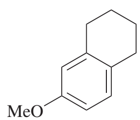
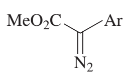
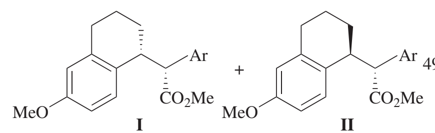
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 2 h	 (71), 74% ee, dr 99:1	79
		Rh_2(*R*,*S*-DOSP)$_4$ (1.0 mol %), hex, rt, 2 h	 (48), dr 88:12	79
		Rh_2(*R*,*S*-DOSP)$_4$ (1.0 mol %), hex, rt, 2 h	 (44), dr 85:15	79
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 (62), dr >97:3	92
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 (25), dr —	92

		1. $Rh_2(S\text{-DOSP})_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h 2. TFA, DCM	 (62), 98% ee, dr >97:3 Ar = 4-BrC_6H_4	92
		1. $Rh_2(OAc)_4$ (0.5 mol %), DCM, 0° to rt, 2 h 2. DDQ, benzene, rt, 2 h	 (77)	139
		1. Catalyst (*x* mol %), DCM, 0° to rt, 2 h 2. DDQ, benzene, rt, 2 h		
		$Rh_2(S\text{-DOSP})_4$ (**42**) (1.0 mol %), DMB, rt, 3 h	 (59), 75% ee Ar = 4-BrC_6H_4	101
	 2.0 eq	Catalyst (1.0 mol %), 3 h	 **I**	101

R	Catalyst	*x*		
Me	$Cu(hfacac)_2$	1.0	(58)	138
Me	$Rh_2(OAc)_4$	0.5	(60)	139
OMe	$Rh_2(OAc)_4$	0.5	(74)	139

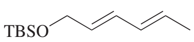
Ar	Catalyst	Solvent	Temp		% ee **I**
Ph	$Rh_2(S\text{-DOSP})_4$ (**42**)	DMB	rt	(60)	83
Ph	$Rh_2(S\text{-DOSP})_4$ (**42**)	DMB	50°	(57)	78
Ph	$Rh_2(S\text{-DOSP})_4$ (**42**)	DCM	rt	(22)	69
Ph	$Rh_2(S\text{-DOSP})_4$ (**42**)	TFT	rt	(53)	84
Ph	$Rh_2(S\text{-DOSP})_4$ (**42**)	TFT	103°	(38)	48
Ph	$Rh_2(S\text{-biTISP})_2$ (**53**)	DCM	rt	(20)	66
4-ClC_6H_4	$Rh_2(R\text{-DOSP})_4$ (**41**)	TFT	rt	(62)	91 *ent*-**I**
4-BrC_6H_4	$Rh_2(S\text{-DOSP})_4$ (**42**)	TFT	rt	(51)	85
4-MeC_6H_4	$Rh_2(S\text{-DOSP})_4$ (**42**)	TFT	rt	(65)	86
4-$MeOC_6H_4$	$Rh_2(S\text{-DOSP})_4$ (**42**)	TFT	rt	(57)	88

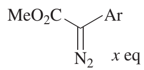
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, rt, 3 h	 (59), 73% ee	101
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, rt, 3 h	 (68), 86% ee	101
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 5 h	 (72), 86% ee	109
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 5 h	 (90), dr 60:40 94% ee (major) 81% ee (minor)	109
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 3 h	 (71), 38% ee, dr 92:8	112
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1.5 h	 **I** + **II**	49

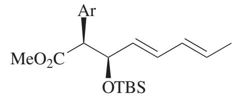
Ar	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
Ph	(77)	17:83	74	94
4-BrC_6H_4	(71)	20:80	—	94

C_{12}



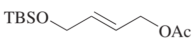


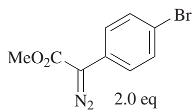
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 1 h



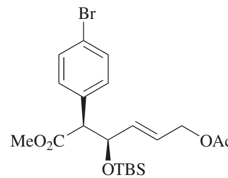
Ar	*x*	Temp		% ee	dr
4-BrC_6H_4	2.0	50°	(92)	79	96:4
4-BrC_6H_4	2.0	rt	(70)	87	96:4
4-ClC_6H_4	—	rt	(71)	74	99:1

90





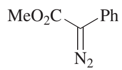
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h



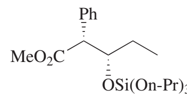
(93), 62% ee, dr >97:3

90

Si(O*n*-Pr)$_4$

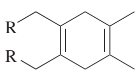


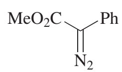
Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), rt, 35 min



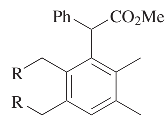
(52), dr >95:5

Solvent	% ee	
DMB	92	82
hex	96	90

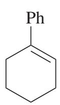


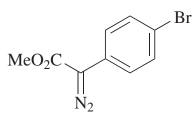


1. Catalyst (*x* mol %), DCM, 0°, 1 h
2. DDQ, benzene, rt, 2 h

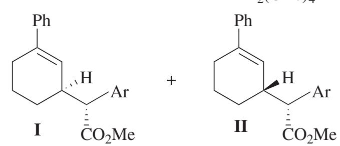


R	Catalyst	*x*		
Me	Cu(hfacac)$_2$	1.0	(55)	138
Me	$Rh_2(OAc)_4$	0.5	(44)	139
OMe	Cu(hfacac)$_2$	1.0	(51)	138
OMe	$Rh_2(OAc)_4$	0.5	(62)	139





Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h



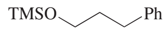
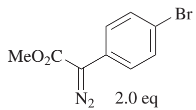
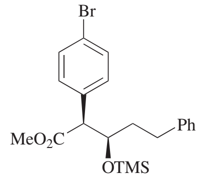
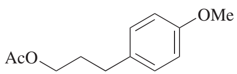
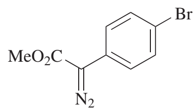
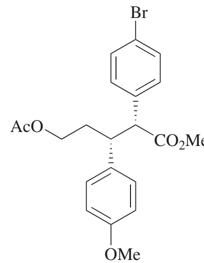
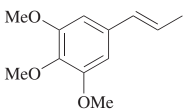
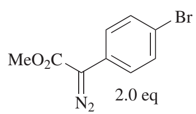
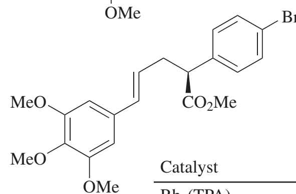
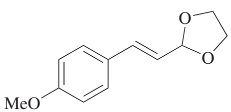
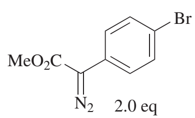
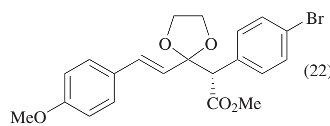
Ar = 4-BrC_6H_4

I + **II** (65), **I**:**II** = 23:77

90% ee **I**, 95% ee **II**

85

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS *(Continued)*

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (41), 89% ee, dr 95:5	90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (75), 76% ee, dr 70:30	90
	 2.0 eq	Catalyst (1.0 mol %), DMB, rt, 5 h		109
	 2.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), TFT, rt, 3 h	 (22), 81% ee	90

Catalyst		% ee
Rh_2(TPA)$_4$	(87)	—
Rh_2(esp)$_2$ (**54a**)	(12)	—
Rh_2(*S*-DOSP)$_4$ (**42**)	(64)	88

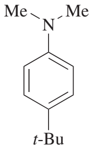
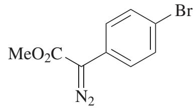
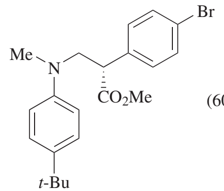
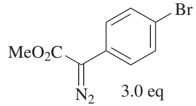
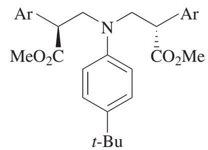
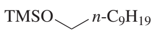
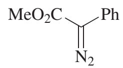
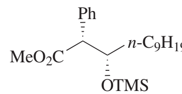
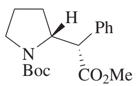
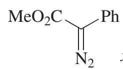
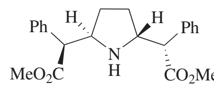
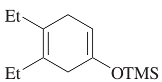
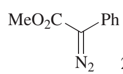
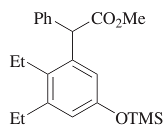
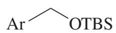
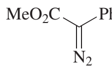
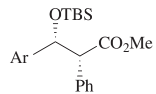
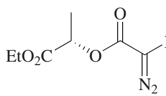
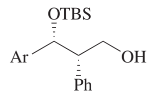
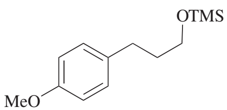
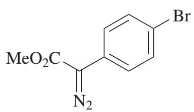
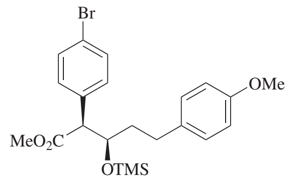
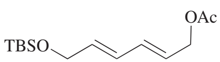
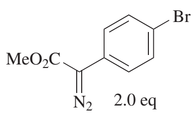
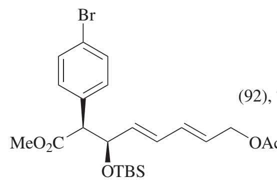
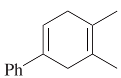
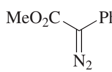
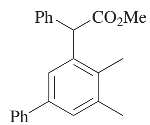
			Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (60), 58% ee	98
		 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (55), 91% ee Ar = 4-BrC_6H_4	98
C_{13}			Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (52), 86% ee, dr 94:6	90
		 *x* eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), solvent, 50°, 4 h 2. DCM, TFA, rt, 2 h		
				x / Solvent / / % ee / dr	
				1.0 / DMB / (45) / 91 / >97:3	86, 92
				4.0 / 2,3-DMB / (93) / >99 / —	80
		 2.0 eq	1. Catalyst (1.0 mol %), DCM, 0°, 1 h 2. DDQ, benzene, rt, 3 h	 Catalyst: Cu(hfacac)$_2$ (33); $Rh_2(OAc)_4$ (35)	138

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
	 2.0 eq	Catalyst (1.0 mol %), DMB, 3 h		112
	 2.0 eq	1. $Rh_2(OOct)_4$ (1.0 mol%), DMB, rt, 3 h 2. DCM, DIBAL-H, 0°		112
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (39), 67% ee dr >97:3	90
C_{14}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (92), 72% ee, dr >97:3	90
	 2.0 eq	1. Catalyst (*x* mol %), DCM, 0°, 1 h 2. DDQ, benzene, rt, 1 h		138, 139

First entry (Ref. 112):

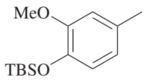
Ar	Catalyst		% ee	dr
Ph	Rh_2(*R*-DOSP)$_4$ (**41**)	(83)	17	96:4
Ph	Rh_2(*S*-PTTL)$_4$ (**38**)	(95)	98	>98:2
4-ClC_6H_4	Rh_2(*R*-DOSP)$_4$ (**41**)	(88)	10	97:3
4-ClC_6H_4	Rh_2(*S*-PTTL)$_4$ (**38**)	(84)	97	>98:2

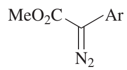
Second entry (Ref. 112):

Ar		% ee	dr
Ph	(69)	84	94:6
4-ClC_6H_4	(91)	82	94:6

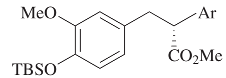
Last entry:

Catalyst	*x*		Refs.
$Cu(hfacac)_2$	1.0	(83)	138
$Rh_2(OAc)_4$	2.0	(70)	139
$Rh_2(OAc)_4$	0.5	(89)	139



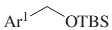


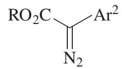
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h



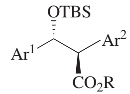
Ar		% ee
Ph	(80)	75
4-BrC_6H_4	(80)	77
4-$MeOC_6H_4$	(30)	67

91





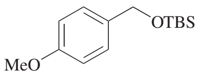
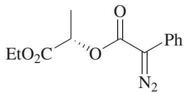
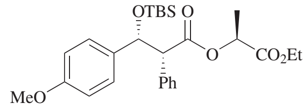
Catalyst (1.0 mol %), 3 h



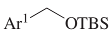
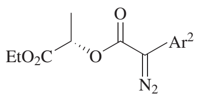
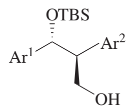
112

Ar^1	Ar^2	R	Catalyst	Solvent	Temp		% ee	dr
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	0°	(81)	31	96:4
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	–40°	(34)	34	95:5
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	rt	(85)	35	94:6
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DCM	rt	(69)	<1	81:19
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	toluene	rt	(67)	24	92:8
4-$MeOC_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	TFT	rt	(51)	35	82:18
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-BNP)$_4$	DMB	rt	(2)	—	72:28
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	rt	(64)	97	96:4
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	50°	(78)	91	95:5
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DCM	rt	(28)	4	75:25
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	TFT	rt	(51)	76	91:9
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-NTTL)$_4$ (**39**)	DMB	rt	(8)	57	83:17
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-biTISP)$_2$ (**53**)	DMB	rt	(82)	69	69:31
4-$MeOC_6H_4$	Ph	Me	Rh_2(*S*-biTBSP)$_2$ (**54**)	DMB	rt	(61)	40	57:43
4-$MeOC_6H_4$	Ph	*t*-Bu	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	rt	(73)	72	89:11
4-$MeOC_6H_4$	4-BrC_6H_4	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	50°	(86)	97	92:8
4-$MeOC_6H_4$	4-$MeOC_6H_4$	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	50°	(88)	96	97:3
4-MeC_6H_4	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	rt	(84)	30	96:4
4-MeC_6H_4	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	50°	(84)	98	97:3
4-$CF_3C_6H_4$	Ph	Me	Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	rt	(74)	30	97:3
4-$CF_3C_6H_4$	Ph	Me	Rh_2(*S*-PTTL)$_4$ (**38**)	DMB	50°	(90)	95	>98:2

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

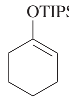
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
		Catalyst (1.0 mol %), 3 h		112

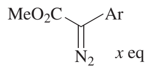
Catalyst	Solvent	Temp		% ee	*syn/anti*
$Rh_2(OOct)_4$	DMB	–78°	(35)	81	6.3:1
$Rh_2(OOct)_4$	DMB	0°	(64)	83	14.4:1
$Rh_2(OOct)_4$	DMB	rt	(83)	79	12.9:1
$Rh_2(OOct)_4$	DCM	rt	(43)	33	1.9:1
Rh_2(*S*-DOSP)$_4$ (**42**)	DMB	rt	(69)	61	5.4:1
Rh_2(*R*-DOSP)$_4$ (**41**)	DMB	rt	(67)	10	8.0:1

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		1. $Rh_2(OOct)_4$ (1.0 mol %), DMB, 3 h 2. DCM, DIBAL-H, 0°		112

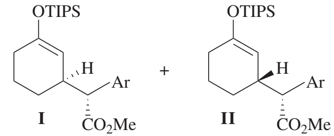
Ar^1	Ar^2	Temp		% ee	dr
4-$MeOC_6H_4$	Ph	0°	(62)	83	94:6
4-$MeOC_6H_4$	Ph	rt	(70)	79	92:8
4-$MeOC_6H_4$	4-BrC_6H_4	rt	(63)	82	91:9
4-$MeOC_6H_4$	4-$CF_3C_6H_4$	rt	(65)	76	90:10
4-$MeOC_6H_4$	4-MeC_6H_4	50°	(65)	68	92:8
4-$MeOC_6H_4$	4-$MeOC_6H_4$	50°	(66)	82	93:7
4-MeC_6H_4	Ph	0°	(35)	86	90:10
4-MeC_6H_4	Ph	rt	(86)	80	90:10
4-$CF_3C_6H_4$	Ph	rt	(89)	85	91:9

C_{15}



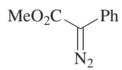


Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, 16 h

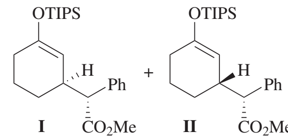


84

Ar	*x*	Temp	**I** + **II**	**I**:**II**	% ee **I**	% ee **II**
Ph	2.0	–30°	(90)	70:30	96	86
4-BrC_6H_4	0.25	–30°	(44)	60:40	95	85
4-BrC_6H_4	0.25	0°	(54)	66:34	92	82
4-BrC_6H_4	0.25	rt	(80)	65:35	90	78
4-BrC_6H_4	2.0	–30°	(86)	65:35	94	84

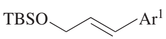


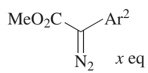
Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt



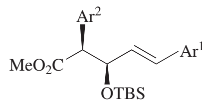
89% ee **I**, —% ee **II**

I + **II** (60) **I**:**II** = 63:37 93





Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 1 h



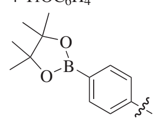
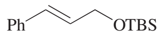
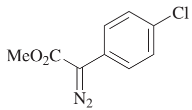
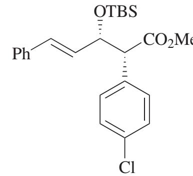
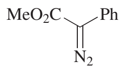
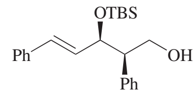
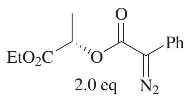
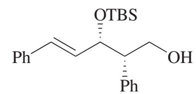
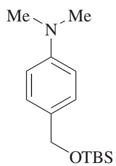
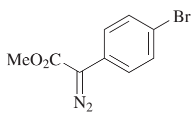
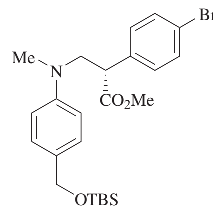
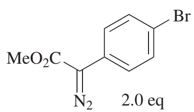
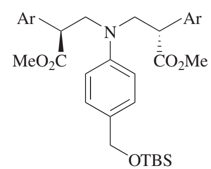
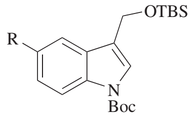
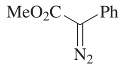
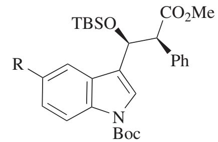
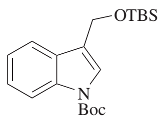
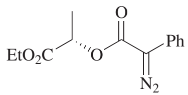
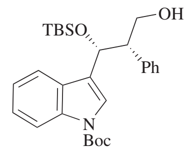
Ar^1	Ar^2	*x*	Temp		% ee	dr	
Ph	Ph	0.5	rt	(73)	77	>97:3	90
Ph	Ph	2.0	–25°	(94)	88	>97:3	90
Ph	Ph	2.0	rt	(98)	74	>97:3	90
Ph	4-ClC_6H_4	0.5	rt	(70)	85	99:1	90
Ph	4-IC_6H_4	2.0	rt	(95)	84	>97:3	107
Ph	4-TfOC_6H_4	2.0	50°	(59)	74	>97:3	107
Ph		2.0	rt	(74)	89	>97:3	107
4-BrC_6H_4	4-ClC_6H_4	0.5	rt	(88)	80	>97:3	90

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 2 h	 (70), 85% ee, dr 99:1	79
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h 2. DCM, DIBAL-H, 0°	 (48), 75% ee, dr >98:2	112
	 2.0 eq	1. $Rh_2(OOct)_4$ (1.0 mol %), DMB, rt, 3 h 2. DCM, DIBAL-H, 0°	 (51), 80% ee, dr >98:2	112
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (70), 61% ee	98
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1.5 h	 (42), 92% ee Ar = 4-BrC_6H_4	98

		Catalyst (1.0 mol %), DMB, 3 h		140

R	Catalyst	Temp		% ee	dr
H	$Rh_2(OOct)_4$	rt	(70)	—	94:6
H	$Rh_2(S\text{-DOSP})_4$ (**42**)	rt	(25)	36	96:4
Br	$Rh_2(OOct)_4$	50°	(60)	—	89:11
Br	$Rh_2(S\text{-DOSP})_4$ (**42**)	50°	(74)	51	85:15
Br	$Rh_2(S\text{-PTTL})_4$ (**38**)	50°	(68)	94	81:19

		1. $Rh_2(OOct)_4$ (1.0 mol %), DMB, rt, 3 h 2. DCM, DIBAL-H		(21), 72% ee	140

C_{16}

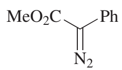
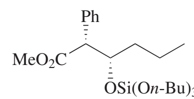
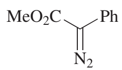
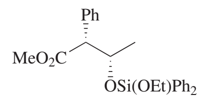
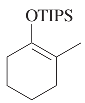
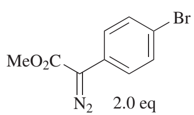
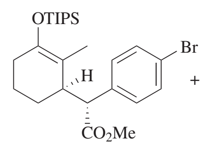
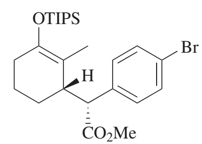
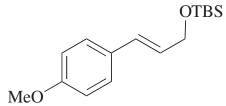
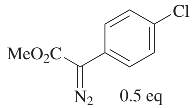
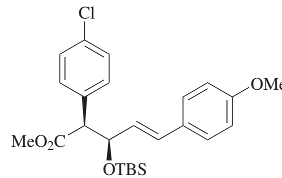
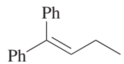
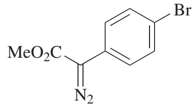
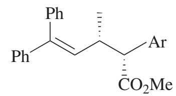
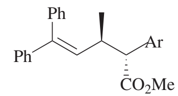
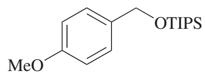
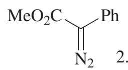
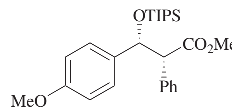
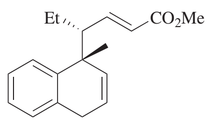
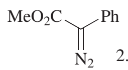
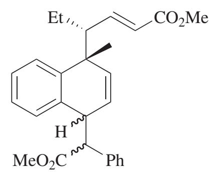
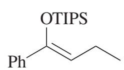
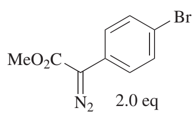
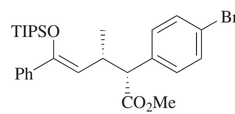
$Si(On\text{-}Bu)_4$		$Rh_2(R\text{-DOSP})_4$ (**41**) (1.0 mol %), rt, 3 h		(58), 93% ee dr >95:5	Solvent: DMB 82; hex 90
$Si(OEt)_2Ph_2$		$Rh_2(R\text{-DOSP})_4$ (**41**) (1.0 mol %), rt, 3 h		(52), 94% ee dr >95:5	Solvent: DMB 82; hex 90
	 2.0 eq	$Rh_2(S\text{-DOSP})_4$ (**42**) (1.0 mol %), DMB, 0°, 16 h	 **I** +  **II** **I** + **II** (81), **I**:**II** = 81:19 89% ee **I**, 88% ee **II**		84

TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}				
	 0.5 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h	 (52), 78% ee dr >95:5	90
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol%), DMB, rt, 2 h	 +  **I** Ar = 4-BrC_6H_4 **II** **I** + **II** (33), **I**:**II** = 85:15 96% ee **I**, 30% ee **II**	85
C_{17}				
	 2.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 3 h	 (46), 15% ee, dr >98:2	57
C_{18}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 (80), dr 20:5:2:1	99
C_{19}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, –30°, 16 h	 (66), 71% ee, dr >95:5	84

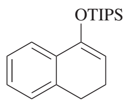
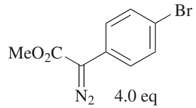
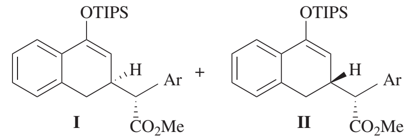
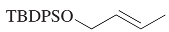
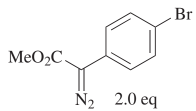
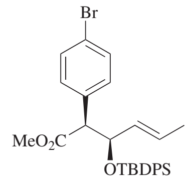
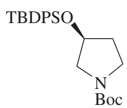
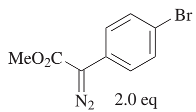
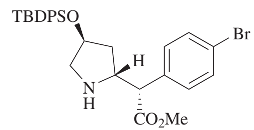
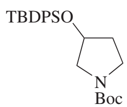
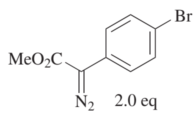
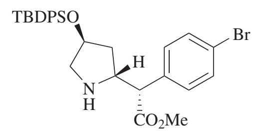
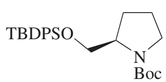
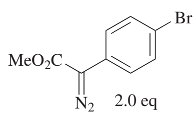
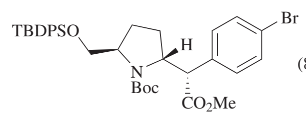
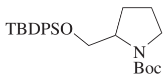
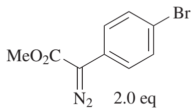
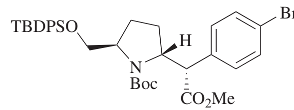
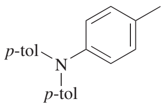
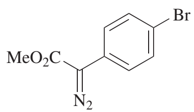
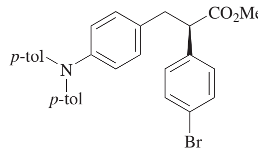
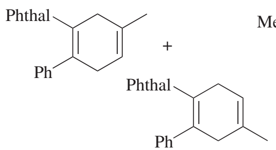
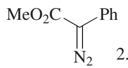
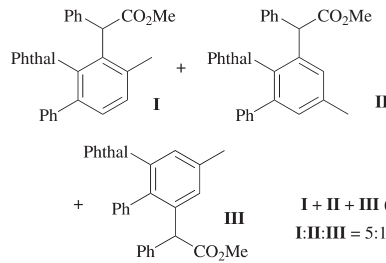
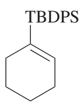
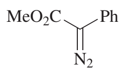
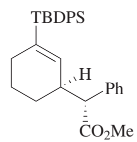
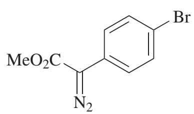
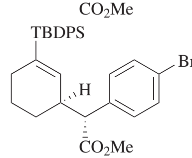
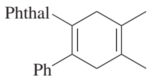
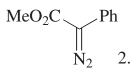
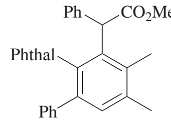
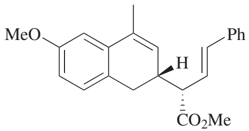
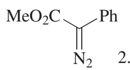
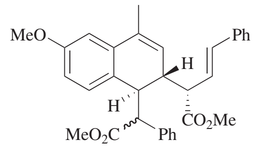
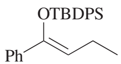
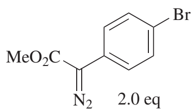
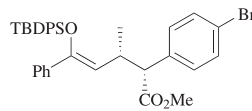
		 4.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, rt, 16 h	 Ar = 4-BrC_6H_4 **I** + **II** (68), **I**:**II** = 74:26 90% ee **I**, 73% ee **II**	84
C_{20}		 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h	 (64), 18% ee, dr >97:3	90
		 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 5 h 2. DCM, TFA, rt, 5 h	 (69), dr >97:3	92
		 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 5 h 2. DCM, TFA, rt, 5 h	 (64), >99% ee dr >97:3	92
C_{21}		 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 4 h	 (85), dr >97:3	86, 92

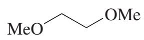
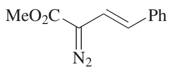
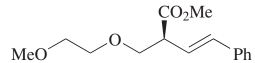
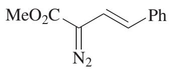
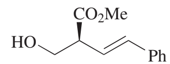
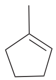
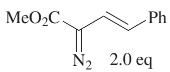
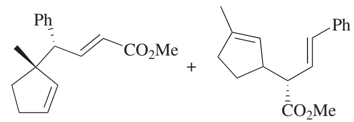
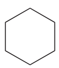
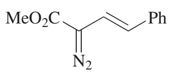
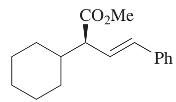
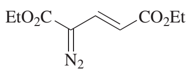
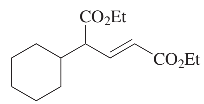
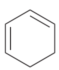
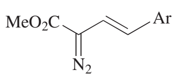
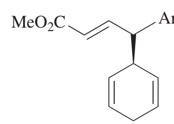
TABLE 3. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM ARYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{21} 	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 2 h	 (85), 98% ee dr >97:3	86
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 35°, 1 h	 (53), 81% ee	91
	 2.0 eq	1. $Rh_2(OAc)_4$ (0.5 mol %), DCM, 0°, 2 h 2. DDQ, benzene, rt, 2 h	 **I** + **II** + **III** (68) **I**:**II**:**III** = 5:10:85	139
C_{22} 		Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), toluene, rt, 18 h	 (62), 94% ee, dr 94:6	93
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 (64), 95% ee, dr 94:6	85

	 2.0 eq	1. Cu(hfacac)$_2$ (1.0 mol %), DCM, 0°, 1 h 2. DDQ, benzene, rt, 3 h		(45)	138
C_{23}					
	 2.0 eq	Rh$_2$(S-DOSP)$_4$ (**42**) (1.0 mol %), TFT/DMB, reflux, 2 h		(86), dr 69:31	99
C_{26}					
	 2.0 eq	Rh$_2$(S-DOSP)$_4$ (**42**) (2.0 mol %), DMB, –30°, 16 h		(65), 84% ee, dr >95:5	84

[a] These values are percent conversions.

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 2 h	 (53), 87% ee	94
C_5 *t*-BuOMe		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 2 h 2. DCM, $MeSO_3H$, rt, 0.5 h	 (38), 95% ee	94
C_6 	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, –20°, 1 h	 (52), 96% ee, dr >99:1 + (43)	57
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), neat, 50°, 1.5 h	 (50), 83% ee	77
		Rh_2(OPiv)$_4$ (2.0 mol %), neat, 81°, 5 min	 (67)	75
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 16 h	 Ar / % ee Ph (63) 98 3,4-$Cl_2C_6H_3$ (59) 99 4-$MeOC_6H_4$ (58) 99 2-$MeOC_6H_4$ (17) 86	81

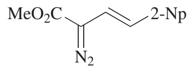
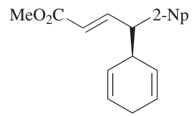
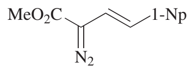
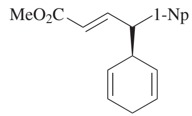
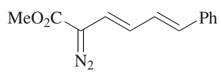
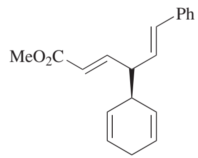
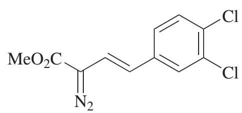
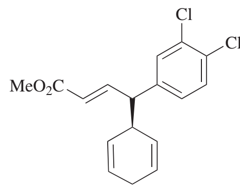
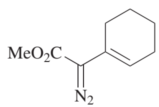
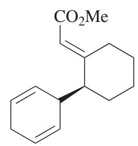
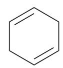
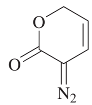
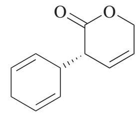
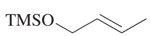
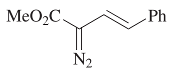
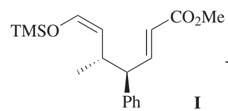
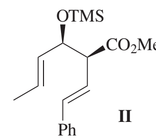
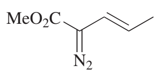
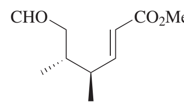
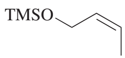
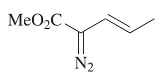
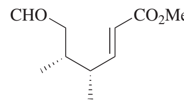
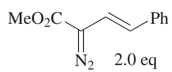
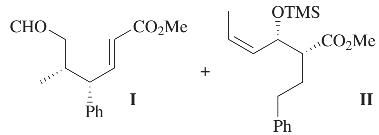
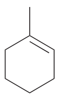
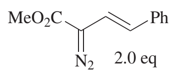
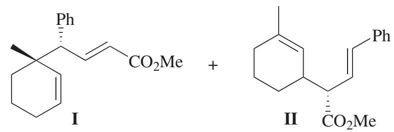
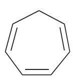
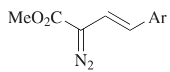
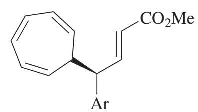
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 16 h		(50), 99% ee	81
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 16 h		(22), 84% ee	81
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 16 h		(60), 99% ee	81
	Immob. Rh_2(*S*-DOSP)$_4$ (**42**) (0.5 mol %), toluene, rt, 20 min		(56), 98% ee	93
	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt, 16 h		(73), 97% ee	81

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS *(Continued)*

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	 2.0 eq	Catalyst (1.0 mol %), DCM, 40°, 9 h		114

Catalyst		% ee
$Rh_2(OAc)_4$	(21)	—
Rh_2(*S*-DOSP)$_4$ (**42**)	(6)	18
Rh_2(*S*-MEAZ)$_4$ (**46**)	(39)	60
Rh_2(*S*,*S*-MenthAZ)$_4$ (**47**)	(38)	79
Rh_2(*S*,*R*-MenthAZ)$_4$ (**48**)	(45)	80
Rh_2(5*S*-MEPY)$_4$ (**49**)	(38)	8

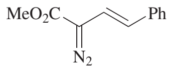
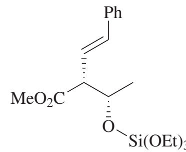
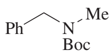
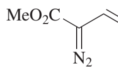
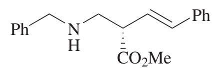
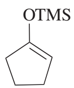
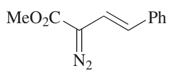
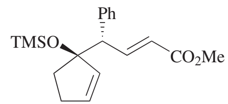
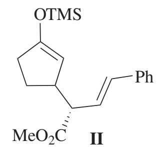
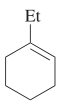
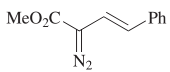
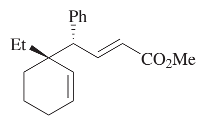
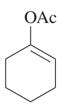
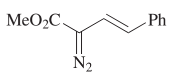
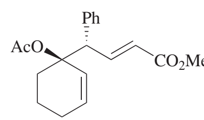
Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h	 **I** +  **II** **I** + **II** (82), **I**:**II** = 1.3:1 91% ee **I**, dr >99:1; 90% ee **II**, dr >99:1	95
		1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h 2. TFT, ionic liquid, 240°, 30 min	 (53), 81% ee, dr >99:1	95

		1. Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 3 h 2. TFT, ionic liquid, 240°, 30 min	 (35), 76% ee, dr >99:1	95
	 2.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 3 h	 **I** + **II** (56), **I**:**II** = 1.2:1 **I** and **II** : 92% ee, dr >99:1	95
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), 1 h		57
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), hex, rt		83

Solvent	Temp	**I** + **II**	**I**:**II**	% ee **I**	dr **I**
DMB	rt	(65)	1.6:1	99	>99:1
TFT	rt	(71)	2.9:1	97	>99:1
TFT	0°	(85)	4.0:1	97	>99:1
TFT	–20°	(65)	4.5:1	98	>99:1

Ar		% ee
Ph	(56)	99
4-BrC_6H_4	(67)	99

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
$Si(OEt)_4$		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), hex, rt, 3 h	 (32), 97% ee, dr 90:10	82
	 2.0 eq	1. Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 4 h 2. DCM, TFA, rt	 (56), 96% ee	88
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, 0°, 1 h	 **I** +  **II** **I** + **II** (6), **I**:**II** = 1:1	57
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, 0°, 1 h	 (31), 95% ee, dr >99:1	57
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, 0°, 1 h	 (55), 98% ee, dr >99:1	57

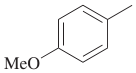
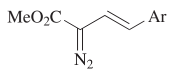
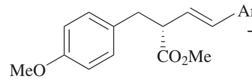
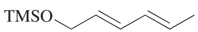
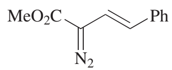
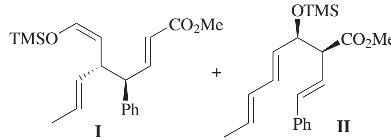
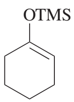
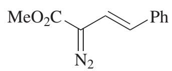
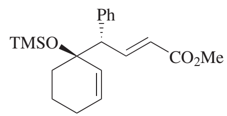
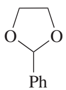
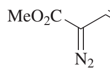
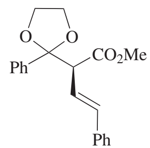
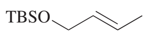
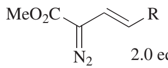
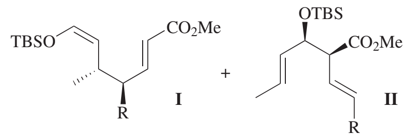
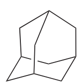
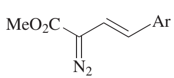
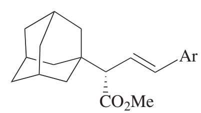
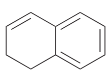
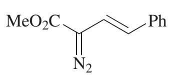
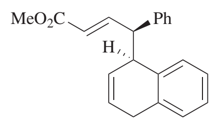
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h	 Ar / % ee Ph (53) 92 4-BrC_6H_4 (51) 94	91
C_9				
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h	 **I** + **II** (85), **I**:**II** = 4.3:1 93% ee **I**, dr >99:1; 91% ee **II**, dr >99:1	95
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT, 0°, 1 h	 (44), 99% ee, dr >99:1	57
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (*x* mol %), DMB, 3 h	 *x* / Temp / % ee 2.0 rt (48) 80 2.0 rt (46) 89 4.0 50° (42) 81	90

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	 2.0 eq	Catalyst (1.0 mol %)		95

R	Catalyst	Solvent	Temp	Time (h)	**I + II**	**I**:**II**	% ee **I**	dr **I**	% ee **II**	dr **II**
Me	Rh_2(*S*-DOSP)$_4$ (**42**)	DMB	rt	4.5	(48)	1.1:1	82	—	81	—
Ph	$Rh_2(OOct)_4$	DMB	rt	3	(36)	1:1	—	—	—	—
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	DMB	rt	3	(90)	1:1	89	>99:1	88	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	DMB	–40°	3	(10)	1:1	92	>99:1	90	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	TFT	rt	3	(68)	2.2:1	76	>99:1	72	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	TFT	–20°	3	(61)	3.1:1	88	>99:1	87	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	toluene	rt	3	(57)	2.4:1	78	>99:1	75	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	toluene	–40°	3	(56)	2.3:1	92	>99:1	89	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	DCM	rt	3	(76)	1.8:1	52	>99:1	48	>99:1
Ph	Rh_2(*S*-DOSP)$_4$ (**42**)	DCM	–40°	3	(35)	2.9:1	70	>99:1	66	>99:1
Ph	Rh_2(*S*-PTTL)$_4$ (**38**)	DCM	rt	3	(12)	1:5	59	—	54	—
Ph	Rh_2(*S*-biTISP)$_2$ (**53**)	DMB	rt	3	(32)	1.1:1	3	—	3	—

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
		Rh_2(*S*-DOSP)$_4$ (**42**) (1 mol %), DMB, 5 h		111
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 1 h	 (67), >99% ee, dr >99:1	97

Ar	Temp		% ee
Ph	69°	(58)	91
4-BrC_6H_4	69°	(57)	95
4-BrC_6H_4	rt	(10)	98
4-$MeOC_6H_4$	69°	(40)	85

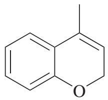
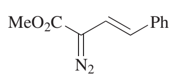
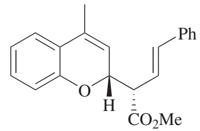
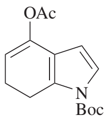
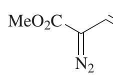
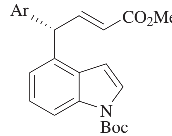
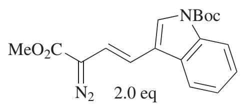
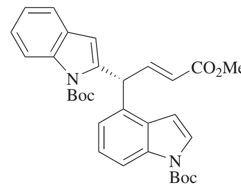
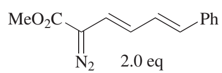
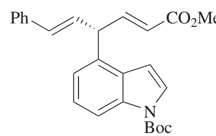
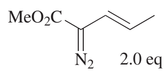
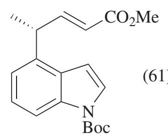
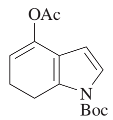
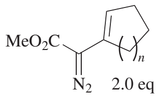
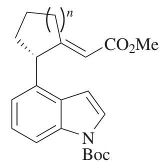
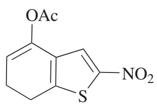
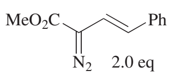
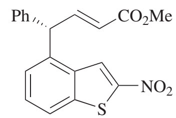
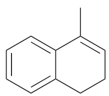
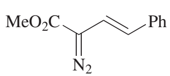
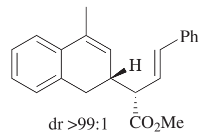
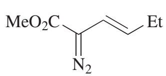
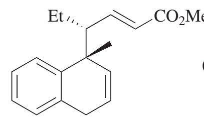
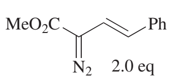
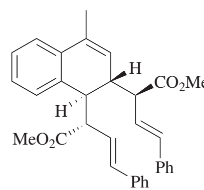
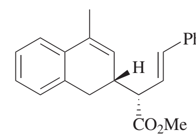
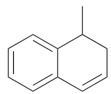
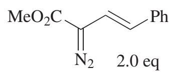
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 1 h		(75), 95% ee, dr >99:1	97
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		Ar — % ee Ph (65) 98 4-BrC_6H_4 (53) 98 3,4-$Cl_2C_6H_3$ (45) 98 4-MeOC_6H_4 (52) 98 2-Np (56) 98	104
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		(64), 97% ee	104
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		(56), >99% ee	104
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		(61), 98% ee	104

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h	 *n* / % ee: 1 (95) 98; 2 (90) 94	104
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h	 (89), >99% ee	104
C_{11}				
		Rh_2(*S*-DOSP)$_4$ (**42**) (*x* mol %), DMB, 12 h	 dr >99:1 *x* / Temp / % ee: 0.1 rt (82) 98; 0.5 0° (95) >99; 1.0 rt (92) 99	97
		Rh_2(*S*-DOSP)$_4$ (**42**) (2.0 mol %), DMB, rt, 2 h	 (57), 98% ee, dr >99:1	97
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 12 h	 (26), 99% ee, dr >97:3 +  (47), 99% ee, dr >97:3	99

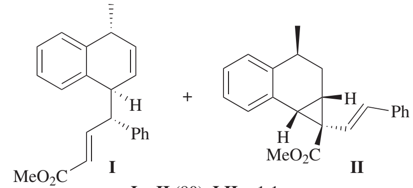
C$_{12}$





2.0 eq

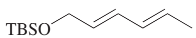
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt

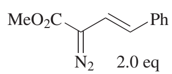


I + **II** (80), **I**:**II** = 1:1

98% ee **I**, 98% ee **II**

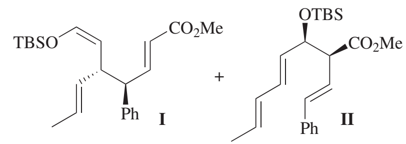
100





2.0 eq

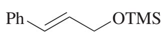
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h

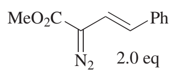


I + **II** (69), **I**:**II** = 2.5:1

92% ee **I**, dr >99:1; 91% ee **II**, dr >99:1

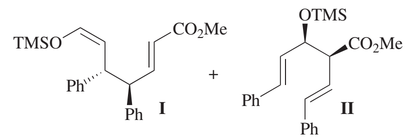
95





2.0 eq

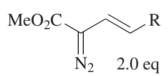
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h



I + **II** (98), **I**:**II** = 1.4:1

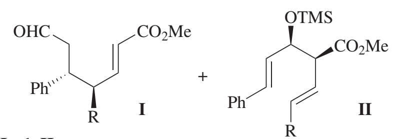
I and **II**: 91% ee, dr >99:1

95



2.0 eq

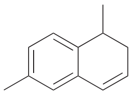
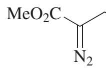
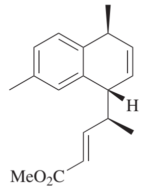
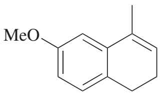
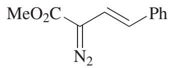
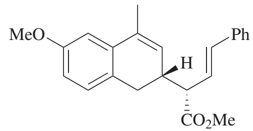
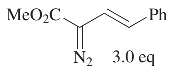
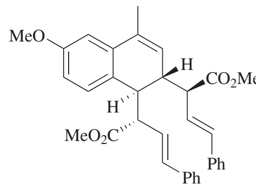
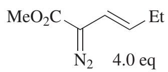
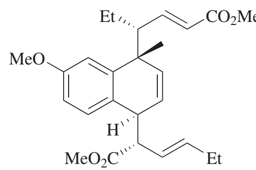
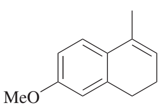
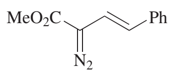
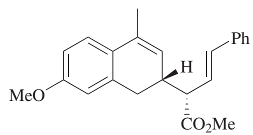
Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h

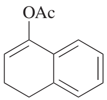
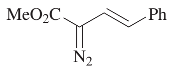
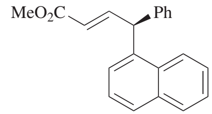
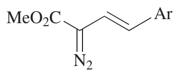
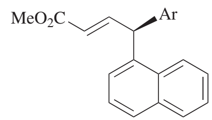


95

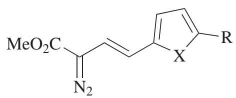
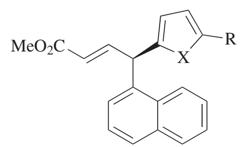
R	**I** + **II**	**I**:**II**	% ee **I**	dr **I**	% ee **II**	dr **II**
Me	(66)	1:1.6	78	>99:1	76	>99:1
Et	(57)	1:2.8	81	>99:1	80	>99:1
CH=CHPh	(73)	1.1:1	83	>99:1	83	>99:1

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}				
	 2.0 eq	Catalyst (2.0 mol %), DMB, rt	 Catalyst / % ee: $Rh_2(OOct)_4$ (22) —; Rh_2(*R*-DOSP)$_4$ (**41**) (36) 90	100
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 12 h	 (97), >99% ee dr >99:1	97
	 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 2 h	 (92), 99% ee dr >97:3	99
	 4.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 2 h	 (56), >99% ee dr >97:3	99
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 12 h	 (90), 99% ee dr >99:1	97

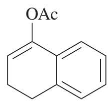
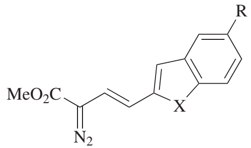
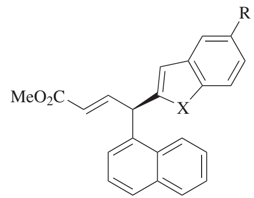
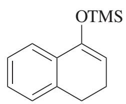
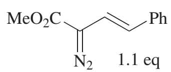
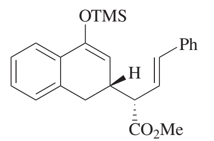
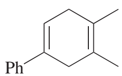
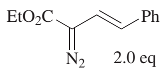
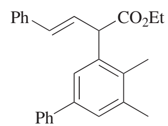
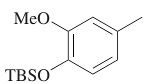
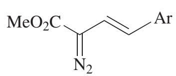
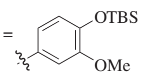
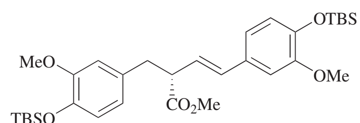
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 1 h	 (85), >99% ee	97
		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), toluene/hex, rt, 13 h		106

Ar		% ee
4-BrC_6H_4	(79)	>99
3,4-$Cl_2C_6H_3$	(79)	>98
4-$MeOC_6H_4$	(82)	>99
3,4-$(MeO)_2C_6H_3$	(92)	99
2-Np	(89)	>98
4-PhC_6H_4	(90)	>98

		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), toluene/hex, rt, 13 h		106

X	R		% ee
O	Cl	(45)	>99
S	H	(14)	—
S	Cl	(88)	>99
S	Ph	(66)	>99

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 		Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), toluene/hex, rt, 13 h	 X / R / % ee: O, H (60) >99; S, H (20) —; NBoc, H (82) >98; NBoc, Br (82) >98	106
C_{13} 	 1.1 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 3 h	 (55), 97% ee, dr >99:1	97
C_{14} 	 2.0 eq	1. $Rh_2(OAc)_4$ (0.5 mol %), DCM, 0°, 1 h 2. DDQ, benzene, rt, 1 h	 (60)	139
	 Ar = 	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 1 h	 (44), 92% ee	91

X	R		% ee
O	H	(60)	>99
S	H	(20)	—
NBoc	H	(82)	>98
NBoc	Br	(82)	>98

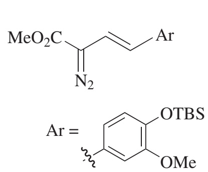
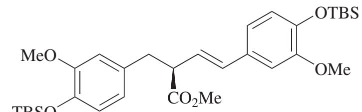
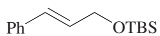
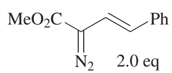
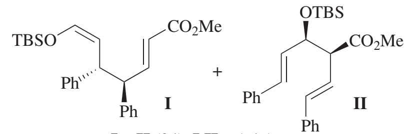
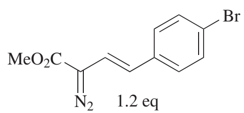
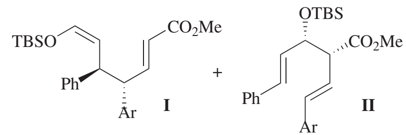
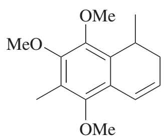
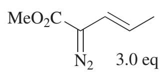
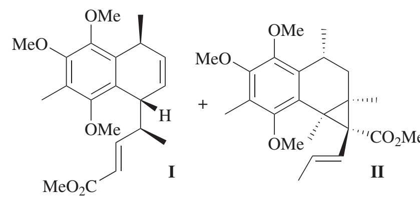
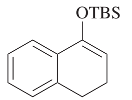
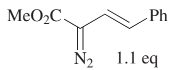
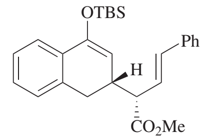
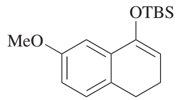
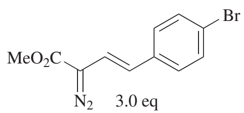
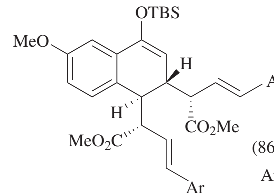
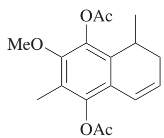
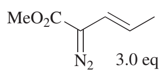
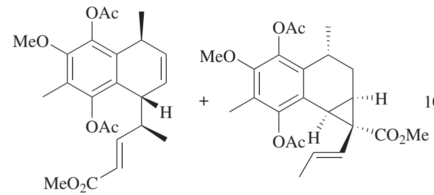
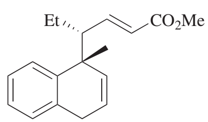
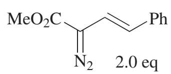
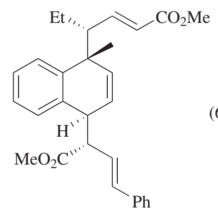
		Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, 50°, 1 h	 (43), 91% ee	91
C_{15}				
	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 3 h	 **I** + **II** (94), **I**:**II** = 1.4:1 **I** and **II**: 91% ee, dr >99:1	95
	 1.2 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (1.0 mol %), DMB, rt, 3 h	 Ar = 4-BrC_6H_4 **I** + **II** (81), **I**:**II** = 1.3:1 90% ee **I**, 89% ee **II**; **I** and **II**: dr >99:1	95
	 3.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (2.0 mol %), DMB, rt, 1.5 h	 **I** + **II** (84), **I**:**II** = 1:1 92% ee **I**, —% ee **II**	103, 102

TABLE 4. C–H INSERTION OF DONOR/ACCEPTOR-SUBSTITUTED CARBENOIDS DERIVED FROM VINYLDIAZO COMPOUNDS (*Continued*)

Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	 1.1 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 3 h	 (78), 95% ee, dr >99:1	97
C_{17} 	 3.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 50°, 2 h	 (86), 99% ee, dr >97:3 Ar = 4-BrC_6H_4	99
	 3.0 eq	Rh_2(*R*-DOSP)$_4$ (**41**) (2.0 mol %), DMB, rt, 1.5 h	 **I** **I** + **II** (92), **I**:**II** = 1:4.7 **II** 89% ee **I**, 30% ee **II**	103
C_{18} 	 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 2 h	 (62), dr >97:3	99

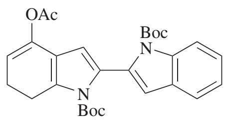
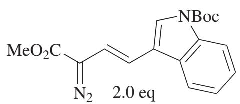
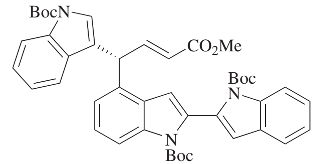
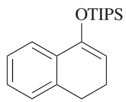
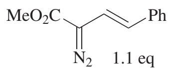
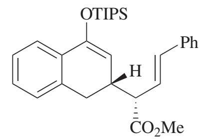
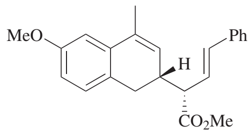
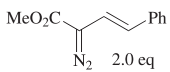
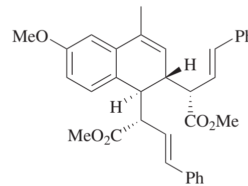
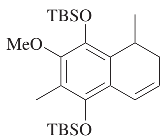
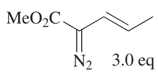
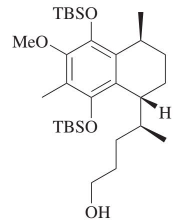
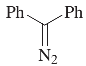
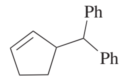
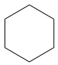
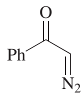
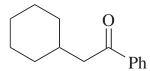
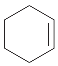
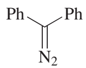
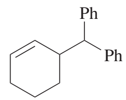
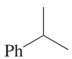
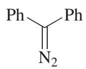
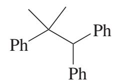
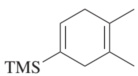
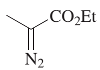
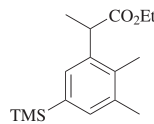
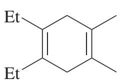
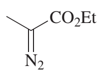
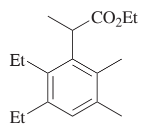
		 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, rt, 1 h		(82), 97% ee	104
C_{19}		 1.1 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), DMB, 0°, 3 h		(53), 91% ee, dr >99:1	97
C_{23}		 2.0 eq	Rh_2(*S*-DOSP)$_4$ (**42**) (1.0 mol %), TFT/DMB, reflux, 2 h		(90), 91% ee	99
C_{25}		 3.0 eq	1. Rh_2(*R*-DOSP)$_4$ (**41**) (2.0 mol %), DMB, rt, 1.5 h 2. EtOH, 10% Pd/C, H_2, 12 h 3. THF, $LiAlH_4$, 0°, 1 h		(34), >95% ee	103, 102

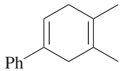
TABLE 5. C–H INSERTION OF CARBENOIDS DERIVED FROM MISCELLANEOUS DIAZO COMPOUNDS

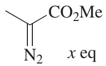
	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5			OsTPFPP (**61**) (1.0 mol %), DCM, 40°, 24 h		(80)	142
C_6			Catalyst (1.0 eq), neat, rt, 0.5 h		Catalyst: $CuSO_4$ (17); CuCl (9)	58
			Catalyst (x mol %)			

Catalyst	x	Solvent	Temp (°)	Time (h)		Refs.
OsTPFPP (**61**)	1.0	DCM	40	24	(83)	142
FeTPFPP (**62**)	100	neat	80	36	(24)	136

	Substrate	Carbenoid Precursor	Conditions	Product(s) and Yield(s) (%)		Refs.
C_9			FeTPFPP (**62**) (1.0 eq), neat, 80°, 20 h		(59)	136
C_{11}			1. $Rh_2(OAc)_4$ (0.5 mol %), DCM, 0°, 2 h 2. DDQ, benzene, rt, 2 h		(55)	138
C_{12}			1. $Rh_2(OAc)_4$ (0.5 mol %), DCM, 0°, 2 h 2. DDQ, benzene, rt, 2 h		(9)	138

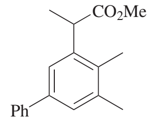
C_{14}





x eq

1. $Rh_2(OAc)_4$ (y mol %), DCM, 2 h
2. DDQ, benzene, rt, 2 h



x	y	Temp (°)		
2.0	0.5	0	(52)	
2.0	2.0	0	(30)	138
3.0	2.0	–18	(59)	
3.0	2.0	0	(58)	

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CHAPTER 3

CROSS-COUPLING WITH ORGANOSILICON COMPOUNDS

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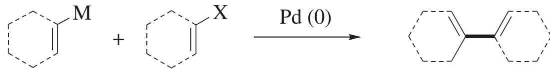
INTRODUCTION

Silicon, an element widely used in many facets of organic chemistry,[1–5] was not effectively employed in cross-coupling reactions until sixteen years after the first reported transition-metal-catalyzed coupling reactions by Corriu[6] and Kumada.[7] Most early developments in this field were achieved through the use of organoboron (1979),[8–10] organozinc (1977),[11,12] and organotin (1977)[13–15] coupling partners (Eq. 1).



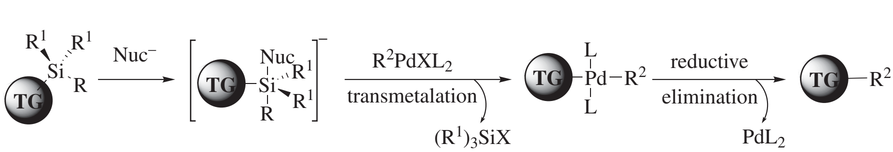
(Eq. 1)

M = SnR_3, BR_3 or $B(OR)_3$, ZnR
X = I, Br, Cl, OTf

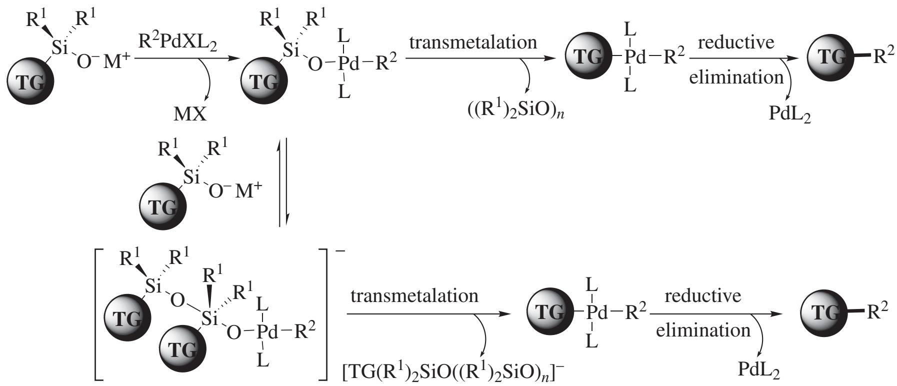
Environmentally benign and of low molecular weight, organosilicon functions possess many properties that make them the ideal donors of organic groups in cross-coupling reactions. However, despite silicon's location in Group 14 along with tin and with similar electronegativity (1.90 for silicon vs. 1.96 for tin),[16] tetracoordinate organosilanes are less capable of transferring one of the attached organic groups to palladium compared with tetracoordinate organostannanes. Despite this limitation, pioneering efforts initiated by several research groups provided the framework on which modern organosilicon cross-couplings are based, namely, that appropriately substituted organosilicon compounds are capable of expanding their valence.[17–20] Through the addition of an appropriate silicophilic Lewis base, an in situ generated pentacoordinate silane can effectively transfer an organic group (TG = transferable group, Scheme 1). This feature allowed for the rapid development of silicon cross-coupling methods that continues today.

In recent years, a new paradigm for silicon-based cross-coupling has been introduced that obviates the need for external activation of the silane. In this scenario, a silanolate salt serves as the carrier and the key transmetalation is facilitated through the formation of a discrete Si-O-Pd linkage. From there, the transferable group migrates with or without additional activation (Scheme 2).

In view of recent advances, organosilicon-based cross-coupling has now become a practical, viable, and in some cases, superior cross-coupling method compared with the more commonly employed organoboron, -zinc, and -tin couplings. The unique properties of organosilicon compounds provide a number of distinct advantages to their use as donors in transition-metal-catalyzed cross-coupling reactions: (1) silicon moieties can be introduced into organic substrates by many general and high-yielding methods for the construction of silicon-carbon bonds, (2) organosilicon reagents are chemically robust and allow isolation and purification of the products and are compatible with many functional groups, (3) silicon-containing byproducts of the coupling are of low molecular weight, are non-toxic, and are easily removed from reaction mixtures, and (4) a number of mild methods for the activation of the organosilicon moieties are now available that are compatible with many functional groups.

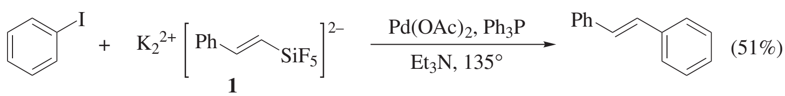


Scheme 1

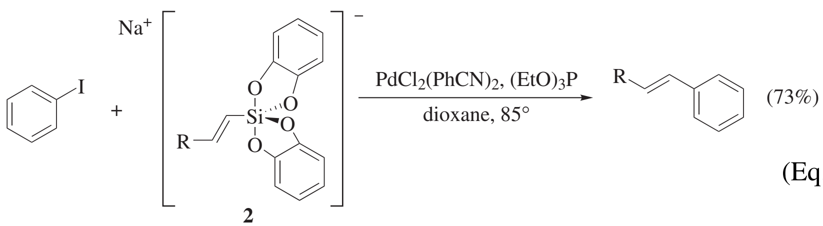


Scheme 2

One of the earliest reports of silicon cross-coupling involves the use of the dipotassium salt of pentafluorostyrylsilicate **1** (Eq. 2).[21] Despite the harsh conditions employed, this reaction provided the first indication that higher-valent silanes could become viable donors in palladium-catalyzed cross-coupling reactions. This concept was further reinforced by the finding that a pentacoordinate silane, sodium alkenylbis(catecholato)silicate **2**, can effectively undergo coupling with several aryl iodides, albeit at elevated temperatures (Eq. 3).[22]



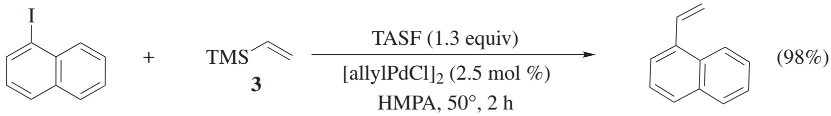
(Eq. 2)



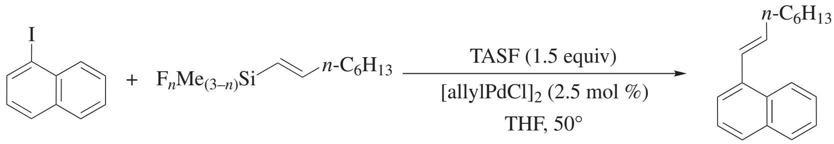
(Eq. 3)

The use of penta- and hexacoordinate silanes illustrates the kind of activation that is required to polarize the carbon-silicon bond sufficiently for a successful cross-coupling reaction. However, the technology at this stage was very limited in substrate scope and reaction efficiency. Beginning in 1988, a series of reports by Hiyama and Hatanaka demonstrated that such limitations can be overcome through the use of an additive to generate the requisite pentacoordinate siliconate moieties in situ (Eq. 4).[23] The substrate scope is significantly expanded when stable and easily synthesized tetracoordinate silanes are used. Nucleophilic fluoride sources are the additive of choice because of the high enthalpy of formation (159 kcal/mol) of a Si−F bond.[24] Yet this modification was not sufficient in all

cases. Whereas vinyltrimethylsilane **3** readily couples with electrophiles in the presence of a fluoride source [tris(dimethylamino)sulfonium difluorotrimethylsilicate or TASF], more substituted alkenyltrimethylsilanes such as **4** do not (Eq. 5).[25] The problem is overcome through the use of the corresponding fluorosilanes **5** and **6**, although **7** is unreactive. Alkoxysilanes **8** and **9** exhibit similar reactivity to fluorosilanes with tetra-n-butylammonium fluoride (TBAF) as the promoter, whereas the trimethoxysilane **10** is less active (Eq. 6).[26]

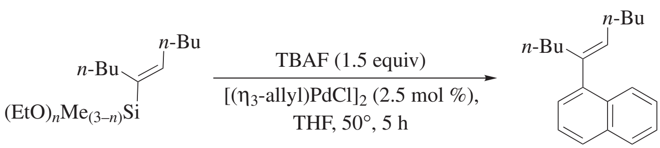


(Eq. 4)



n	Si Reagent	Time (h)	
0	**4**	24	(0%)
1	**5**	10	(81%)
2	**6**	48	(74%)
3	**7**	24	(0%)

(Eq. 5)



(Eq. 6)

n	Si Reagent	
1	**8**	(95%)
2	**9**	(96%)
3	**10**	(54%)

Numerous reports highlighting many permutations of the fluoro- and chlorosilane cross-coupling with aryl, heteroaryl, alkenyl, allyl, and even alkyl halides (or pseudohalides) were published in the following years.[27–30] As shown in Figure 1, this body of work encompassed a wide range of fluorosilane precursors, electrophiles, and even documented multicomponent permutations. These pioneering studies provide a glimpse into the prodigious potential of organosilicon cross-coupling, and therefore suggest that its continued refinement can match the efficiency, selectivity, and versatility of the more actively studied Suzuki-Miyaura coupling of organoboron compounds and the Stille-Migita-Kosugi coupling of organotin compounds.

The next major advance in the evolution of silicon-based cross-coupling was the serendipitous discovery by Denmark that organosilanols can serve as competent partners.[31–35] Silanols are capable of facile cross-coupling under activation

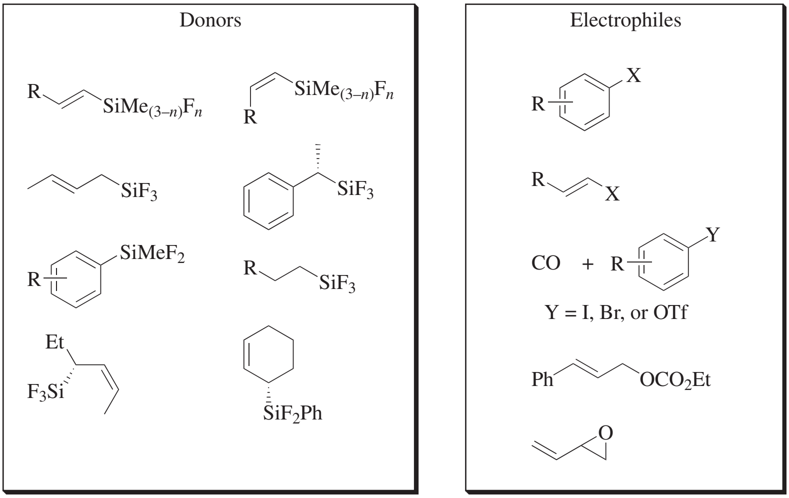
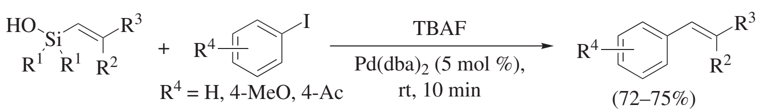


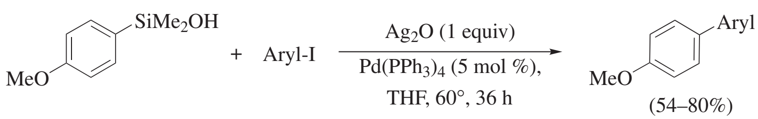
Figure 1. Permutations of organofluorosilane cross-coupling.

by TBAF, but in addition, other promoters such as silver oxide[36,37] and potassium trimethylsilanolate[32] are also effective activators (Eqs. 7–9).

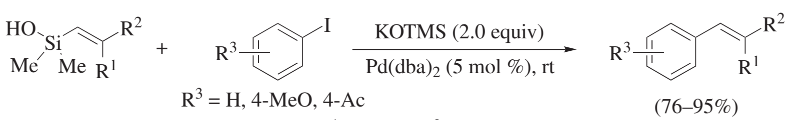


R^1	R^2	R^3	Si Reagent
Me	H	n-C_5H_{11}	(E)-**11**
i-Pr	H	n-C_5H_{11}	(E)-**12**
Me	n-C_5H_{11}	H	(Z)-**11**
i-Pr	n-C_5H_{11}	H	(Z)-**12**

(Eq. 7)



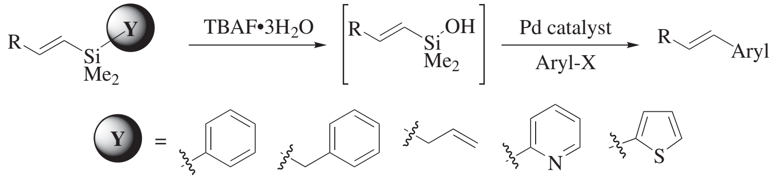
(Eq. 8)



(Eq. 9)

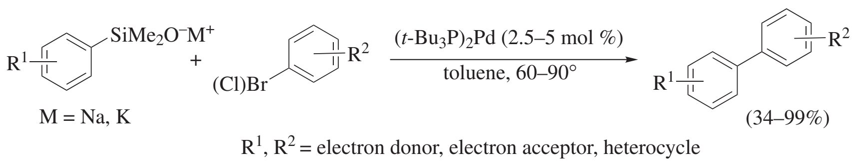
R^1	R^2	Si Reagent
H	n-C_5H_{11}	(E)-**11**
n-C_5H_{11}	H	(Z)-**11**

The demonstration that organosilanols can effectively cross-couple with a variety of organic halides and pseudohalides led to two significant advances: (1) the



Scheme 3

introduction of a myriad of silanol surrogates bearing more chemically robust groups (silacyclobutyl,[38–40] phenyl,[41,42] benzyl,[43–45] allyl,[46,47] 2-thienyl,[48,49] and 2-pyridyl[50–52]) that can be converted into silanols under the action of TBAF•3H_2O (Scheme 3), and (2) the discovery that the conjugate bases of organosilanols (alkali metal silanolates) are the active species under activation by Brønsted bases (Eq. 10).[53,54] These silanolate salts can be generated in situ or prepared and stored as stable solids and are "self-activating" coupling partners.[55] The preparative advantages of the silanolate salts along with the unique mechanism with which they undergo cross-coupling will be described in detail in the following sections.



(Eq. 10)

In contrast to the boron- and tin-based reagents, the diversity of silicon-based reagents that undergo successful cross-coupling is enormous. Silicon moieties bearing three carbon substituents, one, two, or three halogen substituents (both chlorine and fluorine) as well as one, two, or three oxygen substituents (hydroxy, alkoxy, and silyloxy) are all known to participate in cross-coupling reactions with various electrophilic partners. This remarkable diversity reflects the versatility of the silicon-based cross-coupling process. However, this diversity also constitutes an impediment to the practitioner interested in implementing this method, namely, how to select the appropriate precursor for a given transformation.

This chapter presents a thorough overview of the various combinations of transferable groups and organic electrophiles. The scope of the coverage is limited to the combination of silicon-bearing nucleophiles with halo or related electrophiles under catalysis by palladium or nickel complexes wherein the silyl halide (or pseudohalide) is lost. The literature is covered through 2008, with selected references from 2009 and 2010. A number of reviews of silicon-based cross-coupling reactions have already appeared that chronicle the development of the process from the earlier advances with fluoride activation[27–30,56,57] to the more recent improvements[58,59] including Brønsted base-activated silanols[33–35,53,55,60–62] and their application in natural products synthesis.[63]

MECHANISM

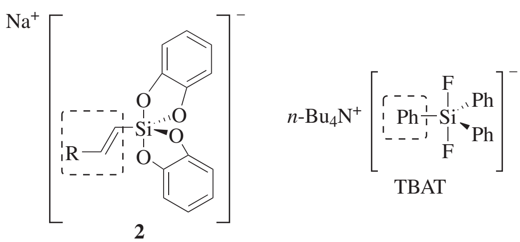
General Catalytic Cycle

The generally accepted mechanism for transition-metal-catalyzed cross-coupling reactions involve: (1) oxidative addition to an electrophilic halide or pseudo halide, (2) transmetalation from an organometallic donor, and (3) reductive elimination to generate a new C–X or C–C bond.[64] Although the oxidative addition of an organic halide to a Pd(0) complex is common among most coupling reactions, the transmetalation step is distinctive to the organometallic donor employed. After transmetalation has occurred, the diorganopalladium species suffers reductive elimination to form the product containing a new carbon-carbon bond and simultaneously regenerates the palladium(0) catalyst.[65,66] The transmetalation step in the cross-coupling of organosilanes has been the subject of stereochemical, spectroscopic, kinetic, and computational studies. For the most part, these studies focus on the catalytic processes that involve activation by fluoride, although two more recent reports address the mechanism of transmetalation of alkali metal silanolates. These two preparatively distinct processes will be discussed separately.

Fluoride Activation via 10-Si-5 Intermediates

The generally accepted paradigm in the field of silicon-based cross-coupling is the necessity to generate a pentacoordinated siliconate as a prerequisite for a successful coupling. This is not an unreasonable scenario because it is well known that silicon can readily expand its valency.[17–20] Although there is no direct evidence for an "activation" step preceding a cross-coupling when a tetracoordinate silane is employed in the presence of a nucleophilic promoter, there is some experimental data that lend support to this contention.[68]

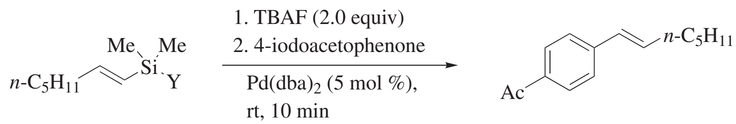
Indirect evidence for an activation step is found in the ability of pre-synthesized, stable, pentacoordinate silanes to transfer an organic group onto palladium. Two examples are the use of catecholsiliconates **2** for alkenyl transfer and the use of tetra-*n*-butylammonium triphenyldifluorosilicate (TBAT) as a phenylating reagent.[21,69–71]



An early observation in the development of fluorosilane cross-coupling noted the effect of heteroatom substitution at silicon on the facility of coupling. In the cross-coupling between (1-octenyl)silylfluorides **5–7**, (Eq. 5) and 1-iodonaphthalene, fluoride substitution on silicon is essential for the coupling to proceed.

The reactivity of the silane decreases with increasing numbers of fluoride atoms, however, such that trifluorosilane (*E*)-**7** is completely unreactive.[25] In a related experiment with alkoxysilanes, a similar effect was observed, with trialkoxysilane (*E*)-**10** displaying reduced reactivity.[26]

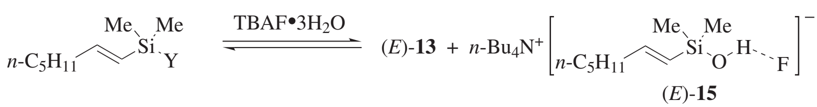
A number of investigations including quantitative evaluation of substituent effects,[72] a Hammett study,[73] determination of a rate equation,[74] and spectroscopic identification of intermediates[75] provided crucial insights into the mechanistic details of the fluoride-promoted cross-coupling reactions. One of the first quantitative comparisons demonstrated that three different monofunctional silanes (silanol (*E*)-**11**; disiloxane (*E*)-**13**; and fluorosilane (*E*)-**14**) react nearly identically under the standard coupling conditions (Eq. 11).



(Eq. 11)

Y	Si Reagent	
OH	(*E*)-**11**	(79%)
$OSiMe_2$–CH=CH–n-C_5H_{11}	(*E*)-**13**	(82%)
F	(*E*)-**14**	(78%)

The similarity of reaction rates and yields results from conversion of all three precursors into a more advanced, common reactive intermediate. ^{29}Si NMR analysis of a mixture of TBAF with either silanol (*E*)-**11**, disiloxane (*E*)-**13**, or fluorosilane (*E*)-**14** show that only two species are formed almost immediately. One was identified as the disiloxane (*E*)-**13** and the other species, (*E*)-**15**, is a hydrogen-bonded complex between the organosilanol and TBAF (Eq. 12). Subsequent kinetic analyses revealed the role of this intermediate in the cross-coupling pathway.



(*E*)-**15**

^{29}Si δ = –8.39 ppm

(Eq. 12)

Y	Si Reagent	^{29}Si δ (ppm)
OH	(*E*)-**11**	–0.30
$OSi(Me)_2C_7H_{13}$	(*E*)-**13**	–3.95
F	(*E*)-**14**	18.40

A cleverly designed Hammett study employing an intramolecular competition between aryl groups in a diaryldifluorosilane revealed a significant dependence on the substituents ($\rho = -1.5$), clearly indicating that the transmetalation step involves electrophilic attack of the arylpalladium(II) intermediate on the *ipso* carbon on the arylsiliconate complex.[73]

Kinetic Analysis and Mechanistic Implications. The kinetic analysis of the TBAF-promoted coupling of (*E*)-**11** with 2-iodothiophene revealed the following

overall rate equation (Eq. 13):

$$\begin{gathered}\text{rate} = k_{obs}[\text{SiOH}]^2[\text{TBAF}]^n \\ k_{obs} = k[\text{Pd}]^1 \\ n = 1 \text{ at TBAF/SiOH} < 2;\ \ n = -1 \text{ at TBAF/SiOH} > 2\end{gathered} \qquad \text{(Eq. 13)}$$

The implications of this equation are detailed below in the context of the basic three-step catalytic cycle for palladium-catalyzed cross-coupling reactions.[64] The first-order rate constant dependence on palladium concentration is consistent with a mononuclear palladium entity participating in each turnover of the catalytic cycle. The zero order behavior in 2-iodothiophene is interpreted as a fast and irreversible oxidative insertion step of the palladium(0) species under the reaction conditions. The ease of this process is well documented and the predominant use of iodides in many of the early reports of cross-coupling chemistry has its origin in this behavior.[64]

The positive correlation between the rate and silanol concentration strongly supports the conclusion that transmetalation is the rate-determining step, as it is in organotin coupling reactions.[15] The unique second-order dependence on silanol concentration indicates that two silicon-based entities participate in the rate-determining transmetalation step. NMR spectroscopic studies revealed the rapid formation of a disiloxane from two molecules of silanol in the presence of TBAF and therefore suggest that the second-order dependence is due to such a disiloxane, not a silanol, undergoing transmetalation.

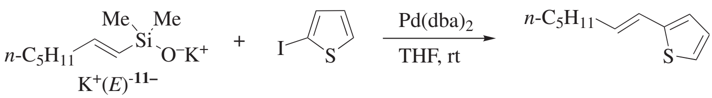
The striking divergence of rate dependence on fluoride concentration is indicative of a change in mechanism. ^{29}Si NMR spectroscopic studies showed that a hydrogen-bonded silanol-TBAF complex (*E*)-**15** is a thermodynamically stable intermediate formed by the interaction of TBAF•3H_2O with nearly any silyl precursor (Eq. 12). If such a complex were formed, then the process of conversion into a pentacoordinated fluoride-activated disiloxane (*E*)-**16** would release one molecule of TBAF for every two molecules of complex initially present (Scheme 4). The intermediacy of (*E*)-**16** and its role in the turnover-limiting, bimolecular transmetalation with the arylPdXL_n species is consistent with the kinetic data (second order in silanol, first order in arylPdX, no kinetic saturation observed) and also consistent with the observed rate dependence on TBAF. Spectroscopic studies showed that at low TBAF concentration, silicon is mostly in the form of disiloxane (*E*)-**13**; however, at higher concentration the predominant species becomes (*E*)-**15**. Direct formation of disiloxane (*E*)-**16** from (*E*)-**11** and resultant fluoride activation would be consistent with second-order behavior in silanol, and first-order behavior in TBAF. However, if all of the silane is present as (*E*)-**15**, then an inverse dependence of the coupling rate on fluoride concentration is expected because one molecule of TBAF must dissociate prior to the rate-determining transmetalation step. Moreover, the mechanistic implications of these studies are also relevant to the TBAF-promoted coupling of fluoro-, hydrido-, and heterocyclic silanes, all of which form related species when mixed with TBAF. In addition, it is likely that hydroxide-activated cross-coupling reactions of monofunctional silanes proceed by a similar mechanism.

However, given the enormous number of competent silane precursors (Figure 3) it would be ill-advised to extrapolate the conclusions from these mechanistic studies to the details of other coupling processes.

A recent computational study on the role of fluoride activation in the cross-coupling of vinyltrimethylsilane **3** with a vinylpalladium(II) complex concluded that prior activation of the silane is energetically prohibitive.[76] Rather, these authors concluded that a termolecular transmetalation transition structure assembly consisting of a complex between **3** and the vinylpalladium(II) species in which fluoride simultaneously activates the trimethylsilyl group is preferred.

Brønsted Base Activation via 8-Si-4 Intermediates

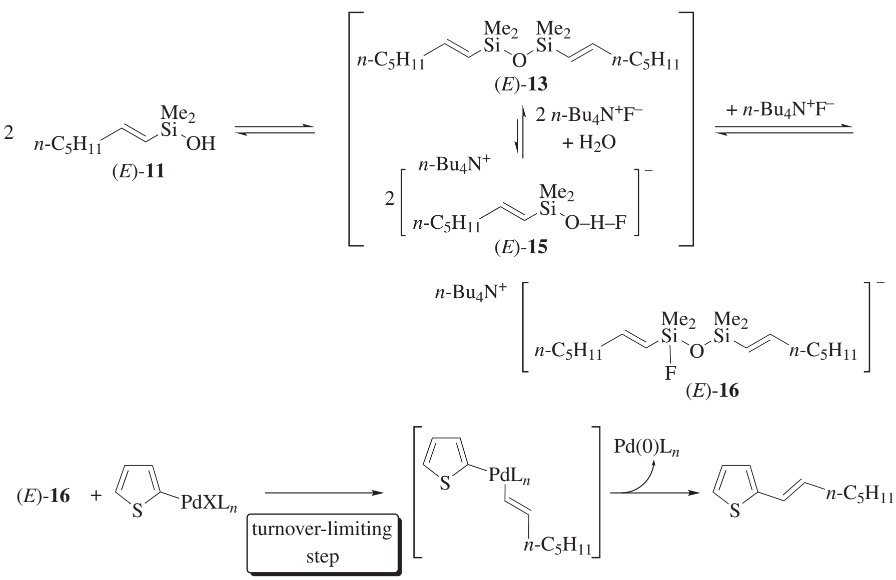
The mechanistic aspects of the fluoride-free cross-coupling reaction of organosilanols and their conjugate bases (Eqs. 9 and 10) have also been investigated.[77] The kinetic analysis examined the coupling of silanolate $K^+(E)$-**11**$^-$ to 2-iodothiophene, which is representative of the KOTMS-promoted cross-coupling of alkenylsilanols (Eq. 14). The derived rate equation is shown in Eq. 15.



(Eq. 14)

$$\text{rate} = k_{obs}[R_3SiOH]^n$$
$$k_{obs} = k[Pd]^1$$
$$n = 1 \text{ when } R_3SiOK/Pd < 20/1;\ n = 0 \text{ when } R_3SiOK/Pd > 20/1$$

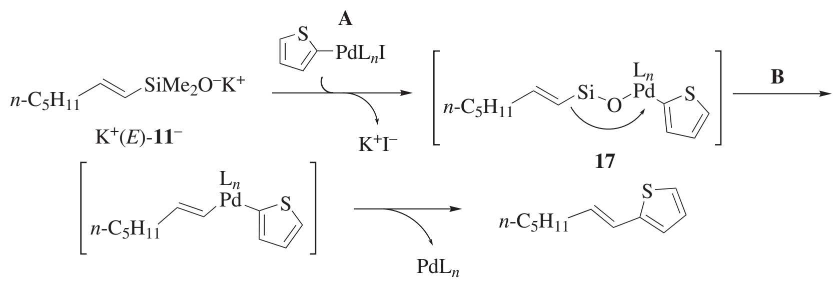
(Eq. 15)



Scheme 4

The zero order rate dependence on 2-iodothiophene and the first-order dependence of the rate constant on palladium concentration are straightforward to interpret. As in the kinetic analysis of the TBAF-promoted system, these data are consistent with a fast and irreversible oxidative insertion of the palladium into the aryl iodide bond. Thus, the oxidative addition step is not interpreted to be the turnover-limiting step of this coupling.

The results of varying the silanolate concentration show two regions with distinct slopes. This behavior is interpreted as a change in the turnover-limiting step. It is immediately apparent that the mechanism diverges from that of the TBAF-promoted reaction. A change to zero order behavior in silanolate is evidence of an intramolecular transmetalation step. The proposed mechanism for this fluoride-free system is, therefore, shown in Scheme 5.



A: displacement is the rate-determing step at R$_3$SiOK/Pd < 20:1
B: transmetalation is the rate-determing step at R$_3$SiOK/Pd > 20:1

Scheme 5

The region of low silanolate concentration (below 20 equiv with respect to palladium) shows first-order behavior, which is interpreted as rate-determining formation of intermediate **17**. This slope levels to a zero order regime at higher silanolate concentrations, which lends support for a rate-determining intramolecular transmetalation from **17**. Because the concentration of palladium catalyst (0.05 equiv with respect to iodide) is static throughout the course of the reaction, a rate-determining intramolecular process involving this catalyst should exhibit a rate behavior independent of silanolate concentration.

The analysis of silanolate order with a stoichiometric amount of palladium with respect to 2-iodothiophene also revealed a first-order dependence of the reaction rate on silanolate concentration.[77] This critical experiment rules out the possibility that an activated complex involving another molecule of silanolate (with **17** to generate a pentacoordinate silicon) is formed. In this latter case, second-order behavior would have been expected.

The demonstration that a neutral, tetracoordinate (8-Si-4) species is capable of rapid transmetalation to an arylpalladium(II) unit forces a revision of the belief that organosilicon donors all require prior activation as a pentacoordinate siliconate. This discovery illustrates the importance of the silicon-oxygen-palladium

linkage because it allows for an otherwise kinetically inaccessible transformation to occur. The divergence of mechanism from that of fluoride activation, wherein an intermolecular transmetalation from a fluoride-activated disiloxane is found to be rate-determining, is remarkable because two equally efficient room-temperature coupling systems can operate via different mechanisms.

Brønsted Base Activation via Both 8-Si-4 and 10-Si-5 Intermediates

The unambiguous demonstration that transmetalation can take place by via both neutral and (8-Si-4) and anionic (10-Si-5) intermediates comes from a recent study on isolated arylpalladium(II) arylsilanolate complexes.[78] The kinetic analysis of the cross-coupling of potassium arylsilanolates with aryl bromides catalyzed by $((t\text{-Bu})_3P)_2Pd$ (Eq. 10) afforded little mechanistic insight (Eq. 16).

$$-d[\text{Aryl-X}]/dt = k_{obs}[M^+\text{ArylSiMe}_2O^-]^0[\text{Aryl-X}]^0 \quad \text{with } k_{obs} = k[Pd]^{0.98} \qquad \text{(Eq. 16)}$$

However, investigation of the stoichiometric process provided a unique insight into the species undergoing the critical transmetalation. Spectroscopic (^1H, ^{13}C, and ^{31}P NMR) and X-ray crystallographic analysis allowed the identification of the key, T-shaped, three-coordinate complex **20** (formed in situ from K^+**18**$^-$ and the oxidative addition product **19**, Figure 2), which undergoes transmetalation with a first-order decay (k_{obs} of 5.0×10^{-4} s^{-1}) to form biaryl **21**. Although this result clearly proves the competence of an 8-Si-4 species to undergo transmetalation, it does not represent the reaction conditions for the catalytic process. In the presence of K^+**18**$^-$, **20** undergoes transmetalation ten-times faster (k_{obs} of 5.0×10^{-3} s^{-1}). Moreover, the rate constant shows a first-order dependence on silanolate, further supporting the conclusion that an activated pathway has intervened. Thus, both pathways can be operative for a given precursor, providing that a palladium silanolate intermediate can be formed.

STEREOCHEMISTRY

Alkenylsilanes

Configurational Specificity. The cross-coupling of alkenylsilanes bearing many different silicon donor moieties with aryl and heteroaryl halides all proceed with high stereospecificity for the formation of geometrically defined alkenes at varying levels of substitution. Examples of (*E*)- and (*Z*)-2-monosubstituted alkenylsilanes are shown in Eqs. 5, 7, and 9. In addition, (*E*)- and (*Z*)-**1**, 2-disubstituted alkenylsilanols[79] and (*E*)- and (*Z*)-2,2-disubstituted alkenylsilanolates[80] undergo clean cross-coupling with high stereospecificity under mild conditions (Eqs. 17a, 17b). Even trisubstituted siloxanes (as in **22**),[81] silanols (masked as in **24**),[45] and silanolates (as in **26)**[80] can produce tetrasubstituted alkenes (**23, 25, 27**) bearing a variety of groups or rings without loss of configurational purity of the starting silane (Eqs. 18a–18c).

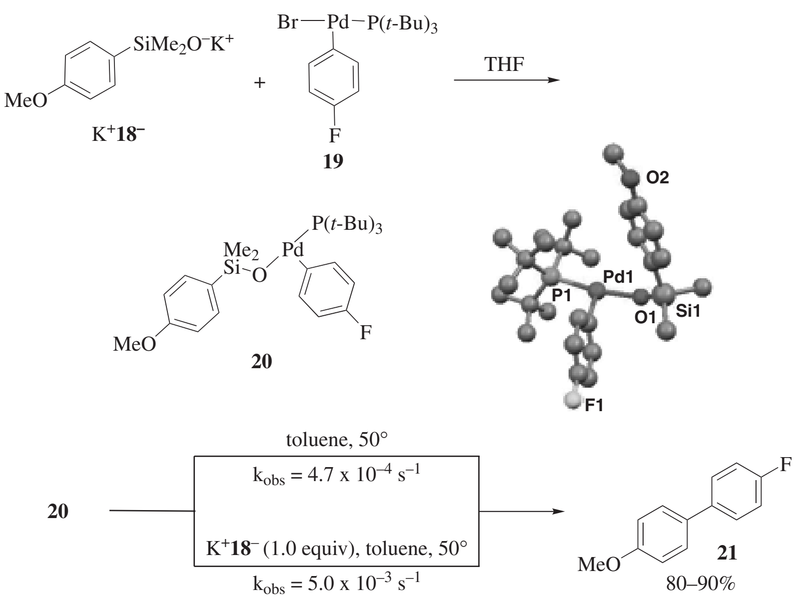
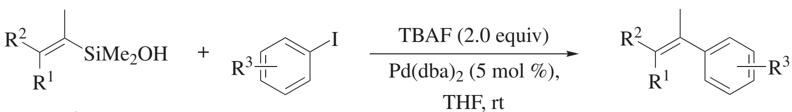


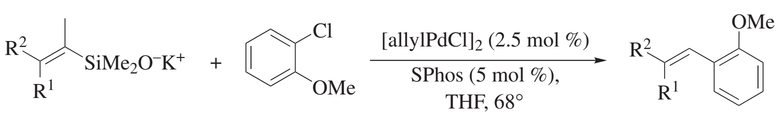
Figure 2. Formation and conversion of an isolable arylpalladium(II) silanolate complex.



R^3 = H, 2-NO_2, 2-CO_2Me, 2-CN, 2-OMe, 4-NO_2, 4-Ac, 4-CO_2Me, 4-OMe

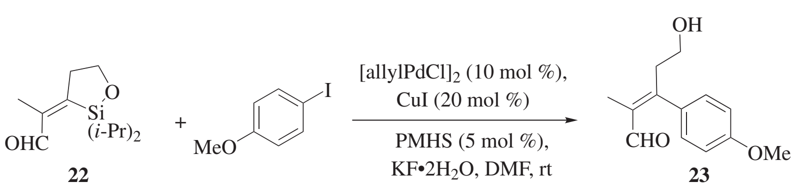
(Eq. 17a)

R^1	R^2	
H	CH_2OTHP	(76–91%), only (*E*)
CH_2OTHP	H	(66–87%), only (*Z*)



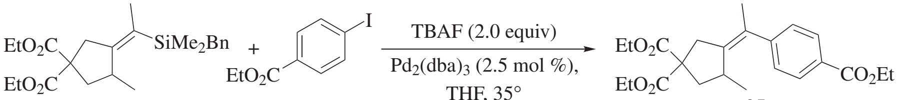
R^1	R^2		(*E*)/(*Z*)
Me	Et	(97%)	98.8:1.2
Et	Me	(89%)	1.4:98.6

(Eq. 17b)



(Eq. 18a)

PMHS = polymethylhydridosilane (83%), only (*Z*)

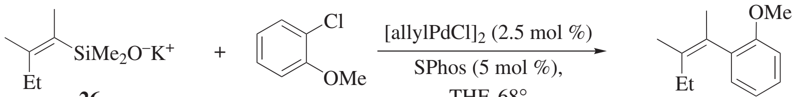


24

25

(72%), only (Z)

(Eq. 18b)



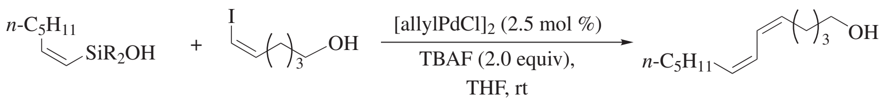
26

27

(95%), (E)/(Z) < 1:99

(Eq. 18c)

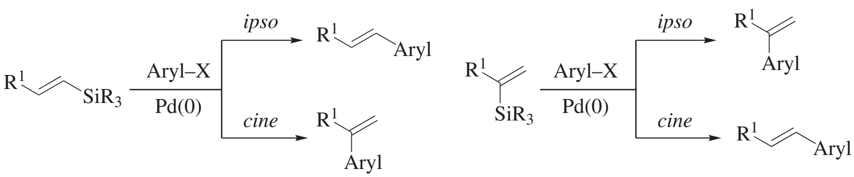
A slight erosion in the geometrical specificity is seen in the coupling of (*Z*)-alkenylsilanols ((*Z*)-**11**, (*Z*)-**12**) (and their surrogates) with (*Z*)-alkenyl iodides (Eq. 19).[31,38] The selectivity can be improved by the use of the diisopropylsilanol.



R	Si Reagent		(Z,Z)/other isomers
Me	(Z)-**11**	(64%)	87.8:12.2
i-Pr	(Z)-**12**	(68%)	92.4:7.6

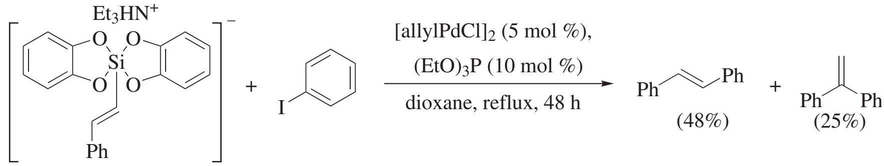
(Eq. 19)

Constitutional Site Specificity. Alkenylsilanes can display the same divergence of site selectivity (*ipso* or *cine*) as is also seen in the cross-coupling of alkenylstannanes[82–85] (Scheme 6). In general, the *ipso* pathway is dominant for most combinations of organosilyl donors and aryl/alkenyl electrophiles, but in some instances *cine* substitution can become the major pathway. Anomalous coupling products have been reported in the cross-coupling of bis(catecholato)alkenylsiliconates **28** (Eq. 20).[86,87] The dependence of the *ipso*/*cine* product ratio on the electronic properties of the aryl electrophile in cross-coupling with **29**



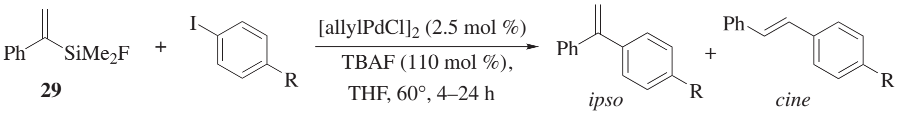
Scheme 6

provides an insight into the structural factors that influenced the mechanistic divergence (Eq. 21).[88,89]



28

(Eq. 20)

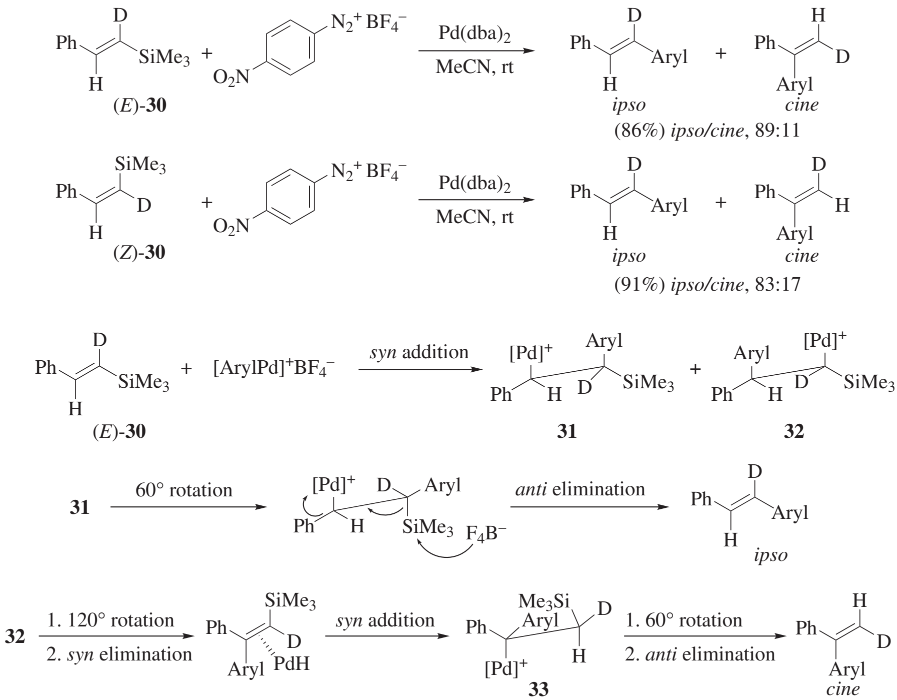


R	*ipso* + *cine*	*ipso*/*cine*
CF_3	(72%)	97:3
H	(69%)	75:25
OEt	(63%)	60:40

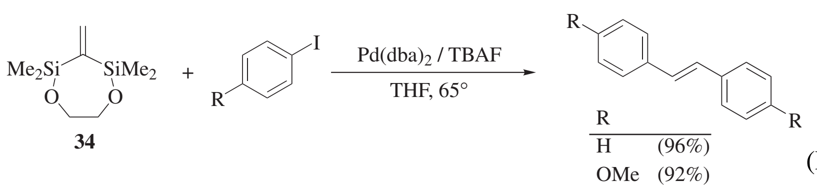
(Eq. 21)

By far the most commonly encountered complications from *cine* substitution pathways occur for alkenyltrimethylsilanes[90−92] and vinyltrimethylsilane in particular. In fact, long before the advent of modern, silicon-based, cross-coupling methods,[23] the divergent behavior of styryl- and vinyltrimethylsilanes in reactions with aryldiazonium salts in the presence of palladium(0) catalysts was demonstrated.[93−97] These studies, employing geometrically defined and isotopically labeled 2-styryltrimethylsilanes (E)- and (Z)-**30**, are interpreted in terms of a Heck-type carbopalladation process that supersedes the expected transmetalation pathway (Scheme 7). Addition of $[arylPd]^+$ across the double bond produced two constitutional isomers, **31** and **32**. Adduct **31** can proceed directly to the *ipso* product by an *anti* elimination of Me_3SiF and Pd(0). Adduct **32** is proposed to undergo a *syn* β-hydride elimination, followed by a *syn* readdition, to form **33**, which then suffers an *anti* elimination of Me_3SiF and Pd(0) to form the *cine* product. The pathway for reaction of (Z)-**30** is similar, but interestingly, the final step to form the *ipso* product must proceed via a *syn* elimination process to explain the formation of the same geometrical isomer from both precursors. Subsequent studies have sought to refine the mechanistic details for reactions of other coupling partners, but the basic concepts remain the same.[98−103]

A particularly dramatic and preparatively useful example of the *cine* rearrangement process involves the double cross-coupling of geminal (bis)silyl ether **34**, which under standard conditions affords the *trans*-stilbenes in excellent yield (Eq. 22).[104] This discovery has also been applied to the synthesis of (E)-poly(arylenevinylene)s by the use of dihaloarene electrophiles.



Scheme 7

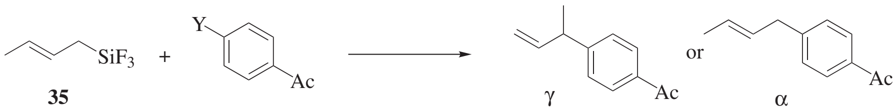


(Eq. 22)

Allylsilanes

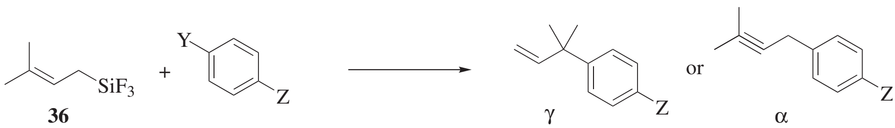
Constitutional Site Selectivity. Allylsilanes are among the most useful organosilicon reagents because of their enhanced reactivity toward a wide range of electrophiles including palladium(II) compounds.[105–107] Accordingly, the catalytic, electrophilic substitution of allylic silanes with organopalladium species should be facile. For simple allylsilanes, no stereochemical or constitutional selectivity issues are extant,[70,108] but allylic silanes bearing substituents on the terminal carbon can have both. For this type of cross-coupling process, allylic trifluorosilanes exhibit high reactivity and selectivity. Both (*E*)-2-butenyl- (**35**) and prenyltrifluorosilane (**36**) react with aryl iodides and triflates to afford substitution products with exclusive γ-site selectivity under activation by TBAF and $(Ph_3P)_4Pd$ or TASF and $Pd(OAc)_2$/dppb, respectively (Eqs. 23a, 23b).[109] The site selectivity of this transformation displays a strong dependence on the ligand such

that with TBAF and (dppp)$PdCl_2$ the α-substitution product is formed.[110]



Y	Conditions		γ/α	(*E*)/(*Z*)
I	$(Ph_3P)_4Pd$, TBAF, THF, 100°, 19 h	(95%)	100:0	—
Br	$(Ph_2P(CH_2)_3PPh_2)PdCl_2$, TBAF, THF, 120°, 12 h	(92%)	0:100	7.2:1
OTf	$(Ph_2P(CH_2)_4PPh_2)PdCl_2$, TASF, THF, 100°, 12 h	(92%)	0:100	7.2:1

(Eq. 23a)

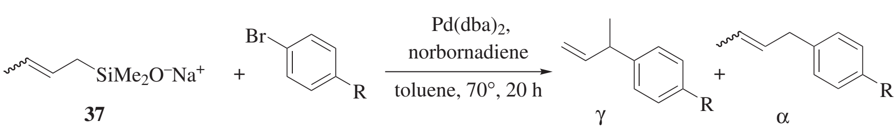


Y	Z	Conditions		γ/α
I	Ac	$(Ph_3P)_4Pd$, TBAF, THF, 100°, 19 h	(70%)	100:0
OTf	CO_2Me	$(Ph_2P(CH_2)_3PPh_2)PdCl_2$, TBAF, THF, 120°, 48 h	(80%)	0:100

(Eq. 23b)

A series of substituted cyclohexenyl and cyclopentenyl benzoates have been studied for the site and stereoselectivity in palladium-catalyzed substitution reactions, including the use of TBAT as a phenylating reagent. The modest selectivities observed are rationalized on the basis of steric effects.[111]

The sodium salt of 2-butenyldimethylsilanol (**37**) also performs well in this process and like the trifluorosilanes also displays a strong dependence of the site selectivity on the ligand.[108] In general, high γ-site selectivities are obtained with catalysts bearing π-acidic ligands such as dba. Norbornadiene assists in catalyst turnover. The scope with respect to the aromatic bromides is broad and the γ-site selectivity is generally higher than 10:1. Interestingly, the use of pure (*E*)-**37** leads to a noticeable improvement in the γ-site selectivity (Eq. 24). The role of π-acidic ligands and double bond geometry are interpreted in terms of a kinetically controlled, γ-selective transmetalation followed by direct reductive elimination to form the branched product (see mechanistic discussion in "Stereospecificity" below).

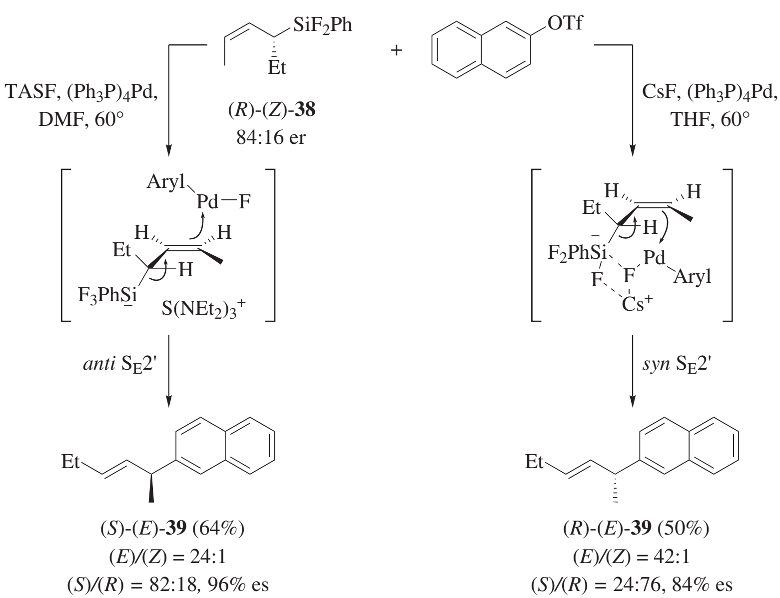


37 (*E*)/(*Z*)	R		γ/α
80:20	PhCO	(81%)	14:1
>97:3	PhCO	(79%)	24:1
80:20	OMe	(46%)	7.2:1
>97:3	OMe	(46%)	18:1

(Eq. 24)

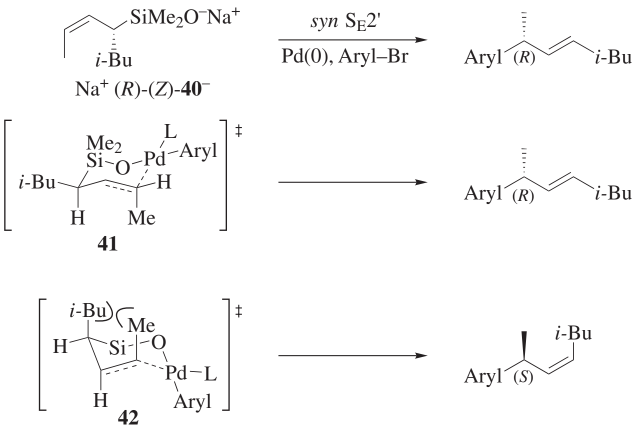
Stereospecificity. In γ-site-selective cross-coupling reactions of unsymmetrically substituted allylic silanes, a new stereogenic center is created. With the aid of enantiomerically enriched and configurationally defined allylic trifluorosilanes and dimethylsilanolates, the stereochemical course of the S_E2' process[112,113] has been elucidated. Enantiomerically enriched allylic difluorosilane (*R*)-(*Z*)-**38**[114] reacts with 2-naphthyl triflate with high γ-site selectivity, but divergent stereospecificity depending on the fluoride source and solvent polarity. With TBAF in DMF, the reaction proceeds in an overall *anti* S_E2' sense (to (*S*)-(*E*)-**39**) whereas with CsF in THF, an overall *syn* S_E2' process (to (*R*)-(*E*)-**39**) is observed (Scheme 8, es = ee (product)/ee (educt) x 100).[115] These results are explained by the operation of an open transition structure for the reaction with TASF and a closed one involving a Pd−F−Si interaction for reaction with CsF.

A similar study revealed a strong and consistent stereochemical correlation for the cross-coupling of enantiomerically enriched allylic dimethylsilanolate Na^+(*R*)-(*Z*)-**40**.[116] In the presence of $[allylPdCl]_2$ and 4,4′-(trifluoromethyl)dibenzylideneacetone, a wide range of aryl bromides undergo highly γ-site selective cross-coupling with perfect *syn* S_E2' stereospecificity (Scheme 9). These results are interpreted in terms of an intramolecular transmetalation via a chair-like, transition structure. In structure **41**, the Si−O−Pd linkage controls the delivery of the palladium electrophile to the γ-terminus of the allylic silane. The palladium is tricoordinate and the alkene takes up the fourth coordination site in the square-planar complex. The pseudo-equatorial orientation of the isobutyl group assures high selectivity in the formation of an (*E*) double bond in the product. In addition, the allylic methyl group is positioned orthogonal to the ligand plane



Scheme 8

of palladium to avoid unfavorable steric interactions. An alternative transition state structure (**42**) that also involves an intramolecular delivery of the palladium moiety suffers from severe 1,3-diaxial steric strain between the isobutyl and allylic methyl groups.



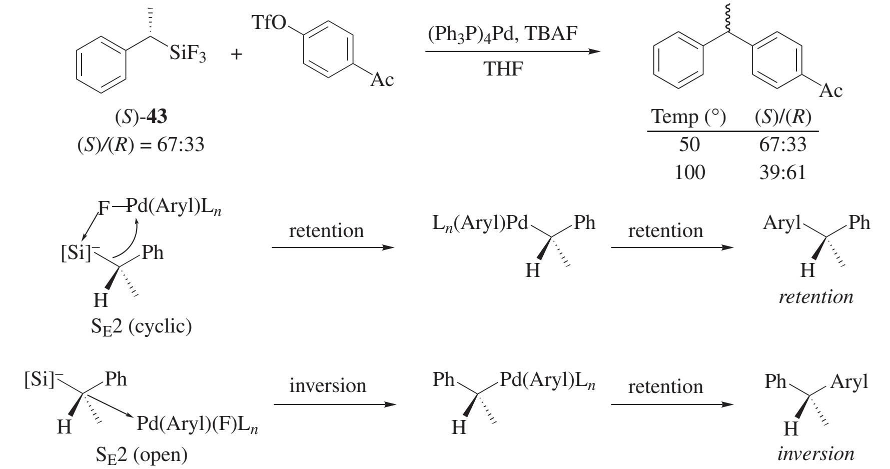
Scheme 9

Benzylsilanes

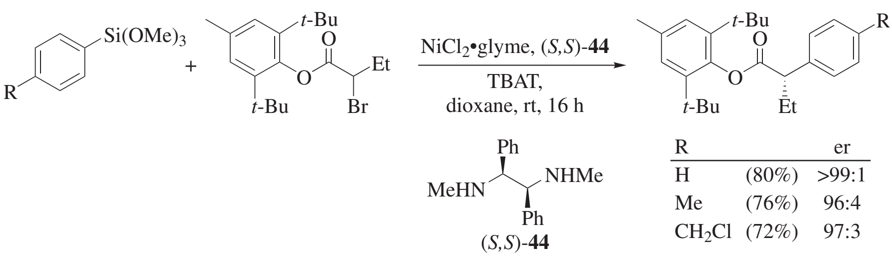
Stereospecificity. The stereochemical course of transmetalation for configurationally defined sp^3-hybridized organosilanes has been studied by the use of enantiomerically enriched benzyltrifluorosilane (*S*)-**43** (Scheme 10).[117] The cross-coupling of (*S*)-**43** with 4-acetylphenyl triflate in the presence of TBAF and $(Ph_3P)_4Pd$ showed an unexpected dependence on temperature and solvent composition. Thus, at low temperature (55°) nearly perfect retention of configuration was observed. As the reaction temperature was increased, the specificity decreased and ultimately changed to inversion with 65% specificity at 100°. These results are interpreted in terms of two competing pathways: a cyclic S_E2 transition structure involving an Si–F–Pd bridge that leads to retention, and an open S_E2 pathway that leads to inversion, the latter being favored as temperature increases.

Enantioselectivity with Aryl- and Alkenylsilanes

The foregoing examples involve the stereochemical consequences of reactions at the silicon-containing moiety in a cross-coupling process. However, silanes also participate in an important transformation in which new stereogenic centers are created by cross-coupling with alkyl halides. Specifically, these nickel-catalyzed reactions involve the combination of aryl- and alkenylsiliconates with racemic α-bromo esters in the presence of a chiral ligand, (*S*,*S*)-**44**, and a fluoride source (TBAT) to provide the α-aryl carboxylic esters in high yields and enantioselectivities (Eq. 25).[118] The stereoconvergence suggests the intermediacy of a configurationally labile organonickel intermediate whose configuration is controlled by the chiral ligand.



Scheme 10



(Eq. 25)

SCOPE AND LIMITATIONS

The diversity of silicon-based reagents that undergo successful cross-coupling is enormous and each has its unique advantages and disadvantages. A complete listing of the types of silicon groupings that have been employed in cross-coupling reactions is shown in Figure 3. Thus, this chapter has been organized with such practical considerations in mind. The "Scope and Limitations" section presents the characteristic strengths and weaknesses of each of the main families of organosilyl donors following the hierarchy shown in Figure 3 (which also constitute the section headings). Within each silafunctional group, the description of the coupling reactions will follow the type of transferable group (TG in Scheme 1) in the order aryl, heteroaryl, alkenyl, alkynyl, allyl, etc. On the other hand, the Tables are organized according to the structure of the transferable group in the order indicated in addition to the organic electrophile. We have presented the field in two complementary frameworks, so that one can learn the salient features of each organosilyl group and find a coupling combination of interest. To avoid confusion in the following presentation, the suffix - silanes will be employed to designate the silafunctional family and the suffix - TGs will be employed to designate the organic group transferred from the silyl moiety.

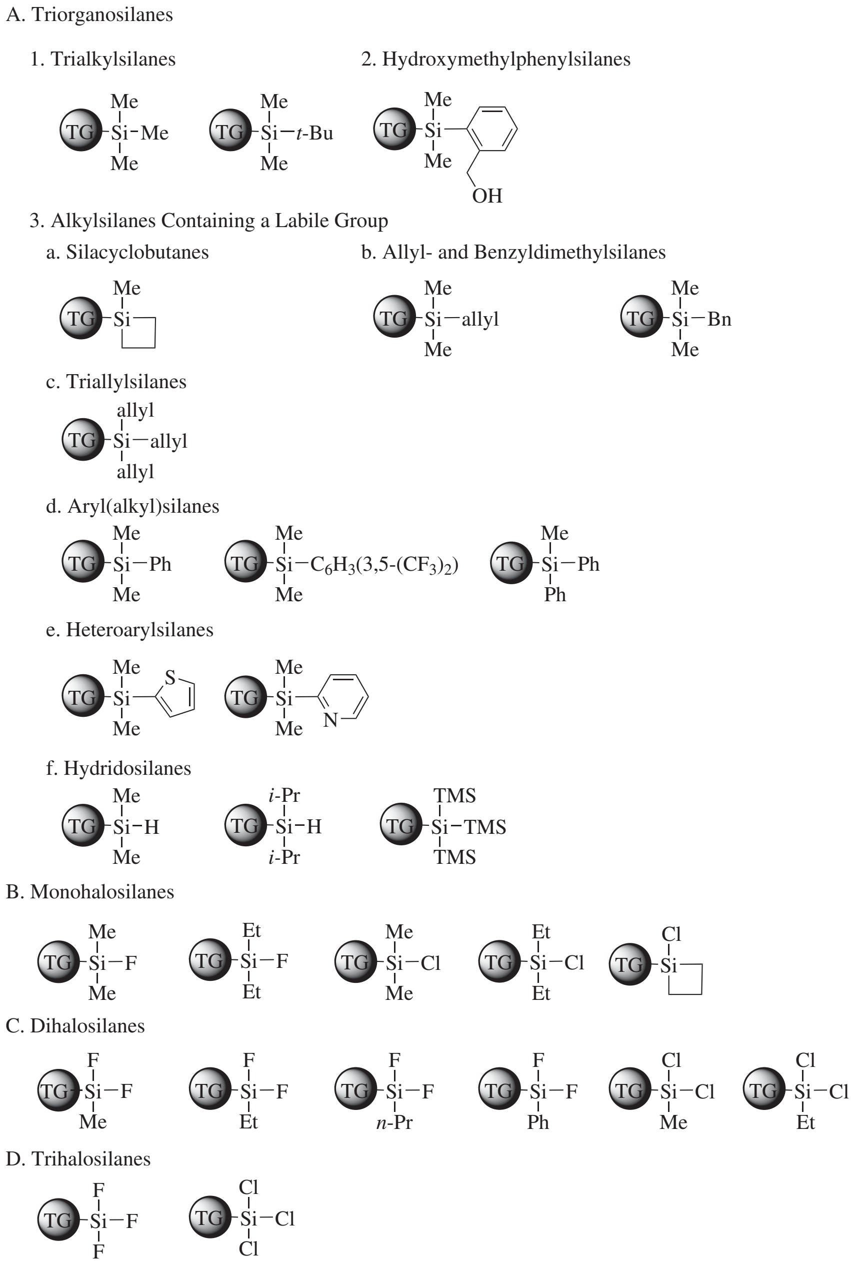


Figure 3. Hierarchy of organosilyl groups used in cross-coupling reactions.

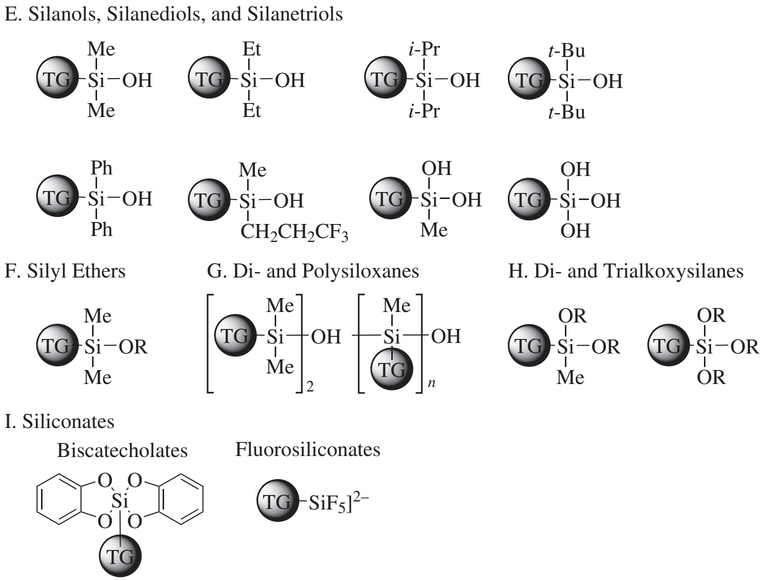


Figure 3. (*Continued*).

Cross-Coupling of Triorganosilanes

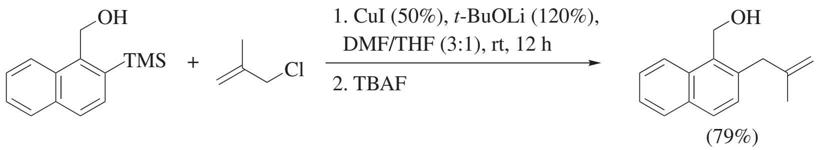
Trialkylsilanes

This category contains silicon moieties bearing only carbon or hydrogen substituents. In some reactions the carbon substituents remain attached to silicon, and in other reactions the substituents are cleaved under the reaction conditions to heterosubstituted silanes.

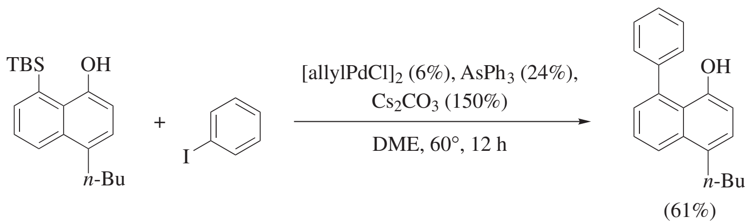
Trimethyl- and *tert*-Butyldimethylsilanes. Despite the fact that these aliphatic organosilane derivatives are the least activated toward formation of the requisite hypercoordinate 10-Si-5 species for rapid transmetalation,[17,20] the number of examples of their cross-coupling reactions is legion. Three different strategies have been developed to activate the triorganosilyl moieties toward transmetalation depending on the nature of the transferable group (TG). For aryl- and alkenyl-TGs, intramolecular activation by an oxyanionic group is commonly employed, whereas for heteroaryl- and simple alkenyl-TGs, activation by an added reagent, usually a fluoride source, is most common. Alkynylsilanes are generally sufficiently reactive that nucleophilic additives are not needed. However, for all of these families of TGs, a copper(I) salt is usually added either in a catalytic or stoichiometric amount. The use of a copper(I) salt implies that the transmetalation step does not take place readily to palladium(II) sources, but rather requires the intermediacy of an organocopper species.

Aryl- and Heteroaryl-TGs. To activate a trialkylsilyl group toward transmetalation, the oxyanionic group is always located in a proximal position, three carbons removed (Eqs. 26a, 26b). In the first example, copper(I) *tert*-butoxide serves as the base and transmetalating agent; allyl and benzyl halides are common

electrophiles in this process.[119] In the second example, a copper(I) salt is not needed, but the temperature is higher for the normal cross-coupling to an aromatic electrophile.[120] The failure of the corresponding methyl ethers to couple supports the need for an oxyanionic activator.

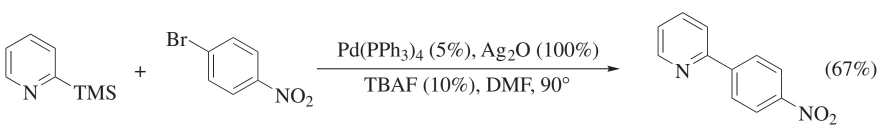


(Eq. 26a)

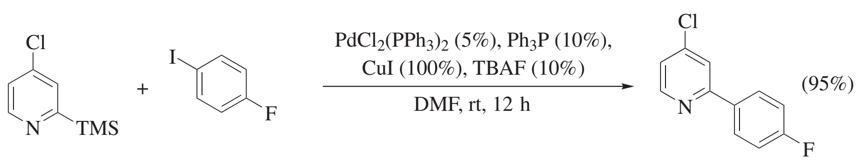


(Eq. 26b)

Although the cross-coupling of 2-pyridyl donor groups is considered to be a major challenge,[121] a wide range of 2- and 3-trimethylsilylpyridines undergo cross-coupling with aromatic bromides and iodides under mild conditions (Eqs. 27a, 27b). Two sets of conditions are available: (1) the use of silver oxide and TBAF as the activator, which requires heating at 90°,[122] or, (2) the use of copper iodide and TBAF, which promotes reactions at room temperature.[123]



(Eq. 27a)

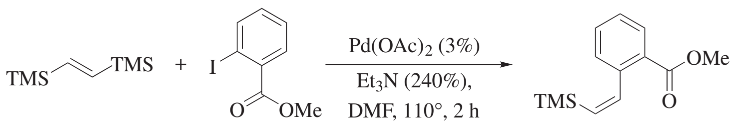


(Eq. 27b)

Alkenyl-TGs. Alkenyltrimethylsilanes can engage in cross-coupling using both external (fluoride) and internal (oxyanion) activation. Donation of a simple vinyl-, 1,3-butadienyl-, or (*E*)-styryl-TG can be accomplished under fairly mild conditions with TASF as the activator. Both aryl and alkenyl iodides are the typical electrophiles, and the couplings are stereospecific.[23,89,124] With aryldiazonium salts as the electrophiles, a significant amount of the *cine* rearrangement product is formed (c.f. Scheme 7).[91]

(*E*)-1,2-Bis(trimethylsilyl)ethene can undergo single substitution to afford styrylsilanes without the need for anionic activators, albeit at 110° in DMF

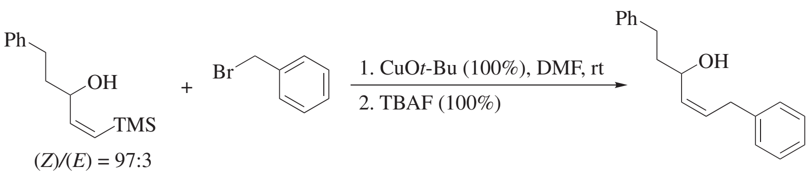
(Eq. 28).[101] Remarkably, the products are predominantly of the (Z)-styryl configuration arising from a *syn* carbopalladation and *syn* silyl depalladation. Additionally, (E,E)-1,4-bis(trimethylsilyl)butadiene and (E,E,E)-1,6-bis(trimethylsilyl) hexatriene can undergo monosubstitution to provide polyenes and styrenes with iodides and diazonium salts.[90,91,124,125] However, these reactions involve an initial electrophilic substitution of the TMS group with BCl_3. Thus, the cross-coupling process does not rigorously involve the TMS group and will not be discussed further.



(Eq. 28)

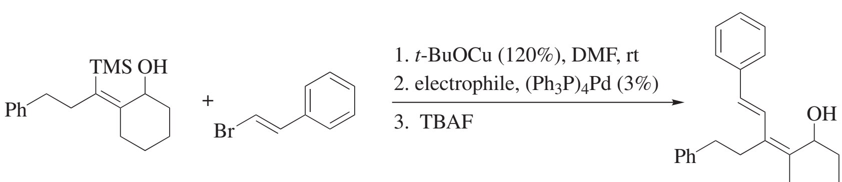
(49%) (Z)/(E)/*cine* = 96:2:2

Oxyanion-assisted cross-coupling of alkenyl-TGs universally employs a *cis* disposition of the TMS group with an alkoxide three atoms removed. In all cases a stoichiometric amount of preformed copper(I) *tert*-butoxide is employed to generate the copper alkoxide that effects the transmetalation. For allylic and benzylic electrophiles, no palladium is needed for the cross-coupling, whereas $(Ph_3P)_4Pd$ is added for alkenyl and aryl electrophiles (Eqs. 29a–29c).[126–128] This strategy was put to good use to generate a trisubstituted alkene by TBS group transfer and methylation in a synthesis of dolabelide D.[129] An interesting modification of this transformation employs a copper enolate derived from 3-trimethysilyl enones.[130]



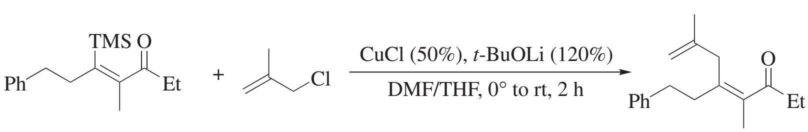
(60%)

(Eq. 29a)



(72%)

(Eq. 29b)

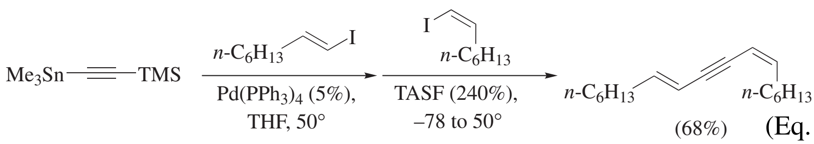


(76%)

(Eq. 29c)

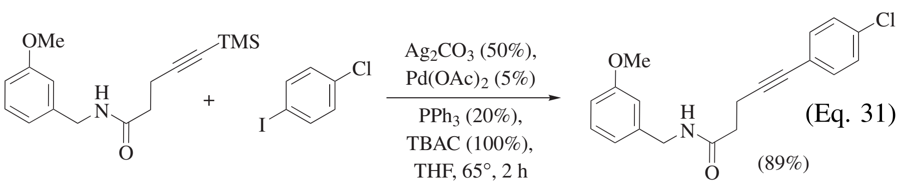
Alkynyl-TGs. By a wide margin, the cross-coupling of alkynyltrimethylsilanes represents the largest application of simple trialkylsilanes as organometallic

donors. Trimethylsilylethyne is used to prepare unsymmetrical tolanes[131] whereas bis(trimethylsilyl)ethyne couples to form symmetrical tolanes.[132,133] Moreover, the differential reactivity of tin and silicon has been used to good advantage for the construction of unsymmetrical enynes and dienynes with trimethylsilylethynyltrimethylstannane (Eq. 30).[134]

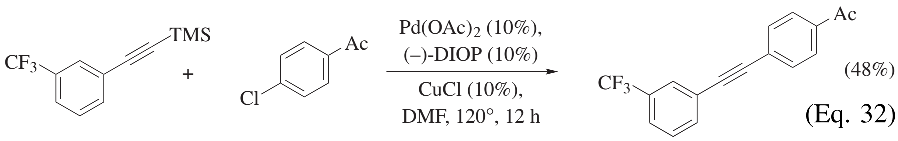


(Eq. 30)

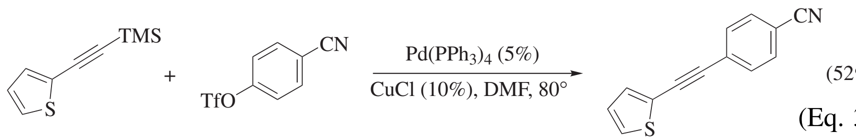
The "silyl Sonogashira" coupling process of trimethylsilyl alkynes has been extensively implemented with a wide variety of electrophiles. The large majority of these reactions employ a copper(I) or silver(I) additive but only a few require a fluoride source. Unlike the original Sonogashira reaction,[135,136] the silyl variant does not require a base to effect the formation of the alkynylcopper species. If a copper-free process is desired, then a fluoride source is added. The number of different recipes for the silyl Sonogashira reaction matches the number of different electrophiles employed. Thus, aryl iodides,[133,137–139] bromides,[140] chlorides,[141] and triflates;[131,133] alkenyl iodides,[139] bromides[23] and triflates;[131,142,143] and alkynyl chlorides[133,144] all use different conditions (Eqs. 31–36).



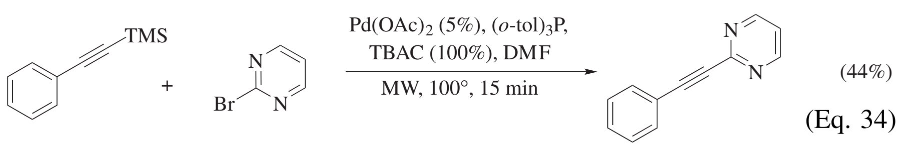
(Eq. 31)



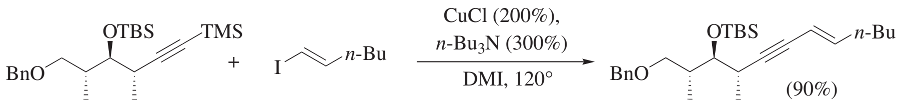
(Eq. 32)



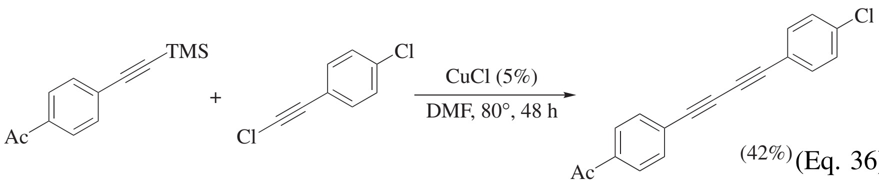
(Eq. 33)



(Eq. 34)

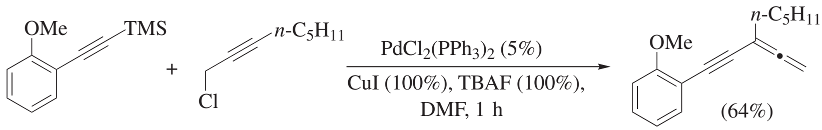


(Eq. 35)

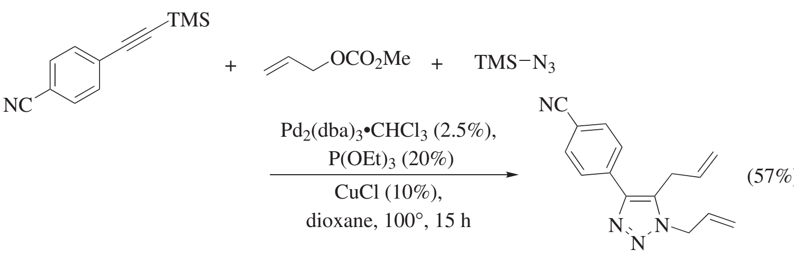


(Eq. 36)

Propargyl chlorides undergo clean S_N2' cross-coupling to afford allenynes (Eq. 37),[145] and allyl carbonates are used in a three-component coupling process to produce diallylated triazoles (Eq. 38).[146] Mechanistically, the cross-coupling may take place on a copper triazole rather than a copper acetylide, but no definitive studies are on record.



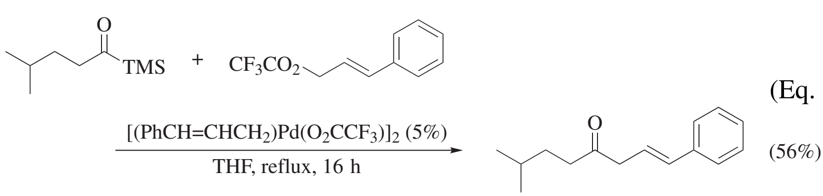
(Eq. 37)



(Eq. 38)

The silyl Sonogashira process is also employed for the synthesis of ethynylene-arylene-ethynylene-thiophene polymers by the use of bis(trimethylsilyl)alkynyl arenes and bisaryl triflates.[147]

Acyl-TGs. One of the most unique examples of a silicon-based cross-coupling is the use of acyl silanes in combination with allylic and benzylic trifluoroacetates (Eq. 39).[148] A palladium(II) cinnamyl trifluoroacetate precatalyst shows the highest activity; phosphines inhibit the reaction and fluoride sources lower the yield.

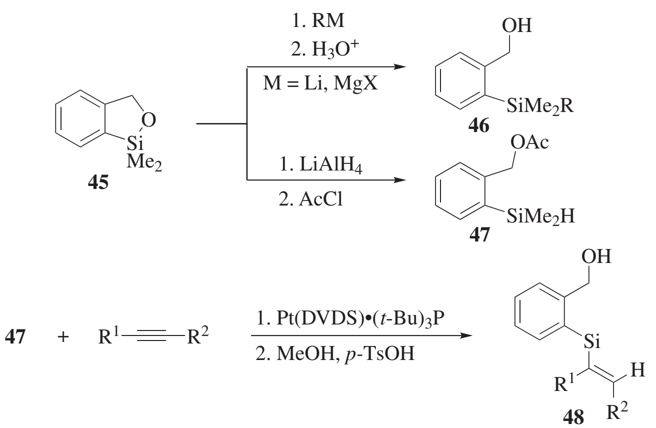


(Eq. 39)

2-Hydroxymethylphenyldimethylsilanes

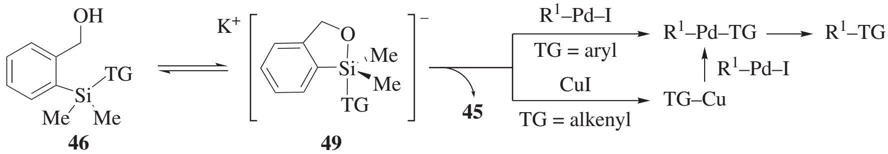
The recognition that intramolecular activation is effective in promoting cross-coupling of simple trialkylsilanes together with a continuing interest in stable and readily available coupling precursors led to the development of a "universal donor" derived from 2-hydroxymethylphenyldimethylsilanes.[149–152] The critical carrier of the various transferable groups is siloxane **45**, which is prepared on a large scale from 2-bromobenzyl alcohol. Introduction of aryl, heteroaryl, and some alkenyl TGs (**46**) is accomplished by reaction of **45** with the corresponding organolithium or -magnesium reagents (Scheme 11). Alternatively, introduction of stereodefined alkenyl TGs (**48**) is accomplished by hydrosilylation of alkynes with hydridosilane **47**, which is prepared by reduction of **45** followed by acylation of the liberated alcohol.

The intramolecular activation by the pendant hydroxymethyl group requires a base such as K_2CO_3, usually in DMSO or blends of DMSO with THF or water. The putative intermediate **49** is believed to exist in a unique trigonal bipyramidal geometry that places the TG in an apical position. In this way, the TG group is transferred preferentially over an equatorial phenyl group. In the cross-coupling of aryl and heteroarylsilanes, copper(I) iodide is added, which might intervene to form an organocopper species prior to transmetalation to the organopalladium intermediate (Scheme 12). The siloxane **45** is a by-product of the cross-coupling and can be recovered in good yield and reused if desired.

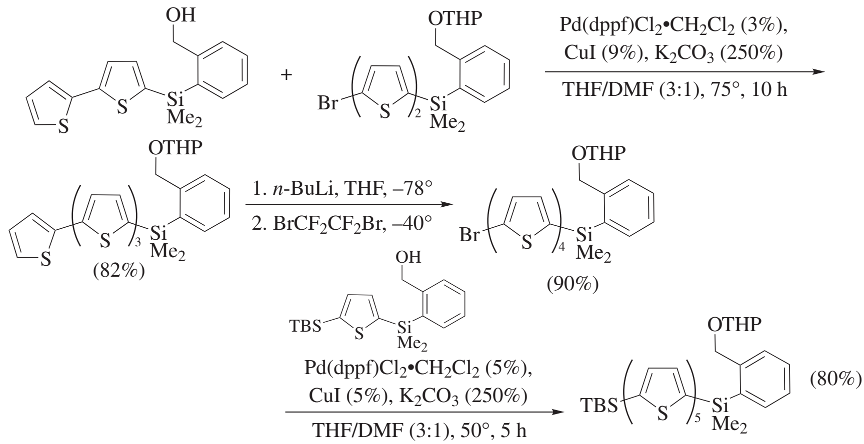


Scheme 11

Aryl- and Heteroaryl-TGs. Aryl groups bearing methyl, fluoro, or diphenylamino substituents undergo cross-coupling with aromatic bromides and iodides as well as with heteroaromatic bromides. Copper(I) iodide is used as a co-catalyst along with $PdCl_2$ or $[allylPdCl]_2$. An iterative cross-coupling procedure has been developed for the synthesis of oligoarenes and oligothiophenes that employs a THP-protected activator that is resistant to the basic cross-coupling conditions and that can be revealed by mild hydrolysis (Scheme 13).[149]

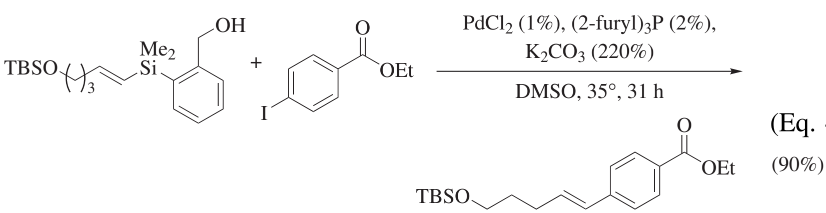


Scheme 12

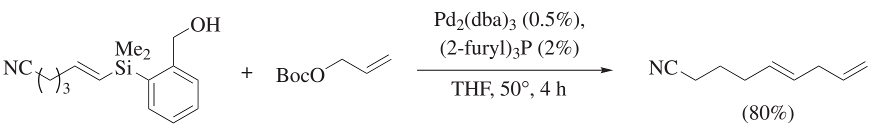


Scheme 13

Alkenyl-TGs. The vast majority of examples in this family employ alkenyl TGs ranging from simple vinyl groups to β-disubstituted vinyl groups to (*E*)-alkenyl groups bearing chloro, hydroxy, silyloxy, acetoxy, cyano, carbomethoxy, or phthalimido functional groups.[150,151] Aryl and heteroaryl iodides are the usual coupling partners, and the reactions are stereospecific. The compatibility of the TBS protecting group illustrates the advantage compared with fluoride activation (Eq. 40). Allylic carbonates participate in the cross-coupling to produce 1,4-dienes without the need for a base activator because the *tert*-butoxide generated in the formation of the π-allylpalladium intermediate serves that role (Eq. 41).[152]



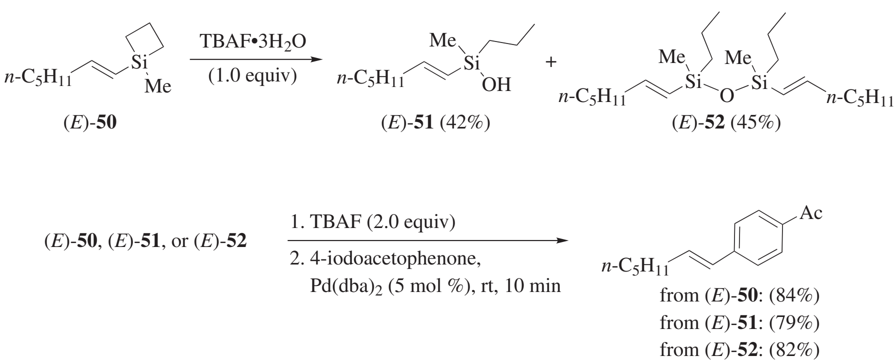
(Eq. 40)



(Eq. 41)

Alkylsilanes Containing One or More Labile Groups

Silacyclobutanes. The original motivation for investigating this somewhat esoteric family of silicon derivatives is founded on the concept of "strain release Lewis acidity"[153–156] as a mechanism for facilitating the ability of tetraorganosilanes to achieve the requisite pentacoordinate state that is believed to be required for rapid transmetalation. Although alkenylsilacyclobutanes undergo highly efficient cross-coupling under fluoride activation, subsequent mechanistic studies revealed that the silacyclobutane ring is spontaneously cleaved on treatment with TBAF•3H_2O to a propylmethylsilanol and its corresponding disiloxanes that are the actual coupling partners. All three of these silane derivatives ((*E*)-**50**, (*E*)-**51**, and (*E*)-**52**) afford the cross-coupling product with equal competency (Scheme 14).[75] This discovery stimulated the investigation of organosilanols and silanolates, which are now among the most versatile silicon-based coupling agents available.



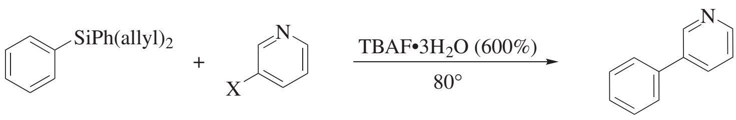
Scheme 14

Alkenyl-TGs. Simple vinyl- and 2-propenylsilacyclobutanes undergo smooth cross-coupling with a variety of aryl iodides under much milder conditions than their trimethylsilyl counterparts. No ligands are necessary in conjunction with Pd(dba)$_2$ and 2−3 equiv of TBAF are used to effect complete conversion in minutes at room temperature.[40] Both (*E*)- and (*Z*)-**50** bearing a pentyl substituent cross-couple readily with aryl and alkenyl iodides in very high stereospecificity and with only trace amounts of the *cine* rearrangement product. Aryl(methyl)silacyclobutanes are not sufficiently activated to undergo cross-coupling, but the arylchlorosilacyclobutane derivatives are; they will be described with other halosilanes.

Allyl- and Benzylsilanes. These silane derivatives also serve as silanol surrogates under activation by TBAF (although they were not recognized as such at the time of their development).

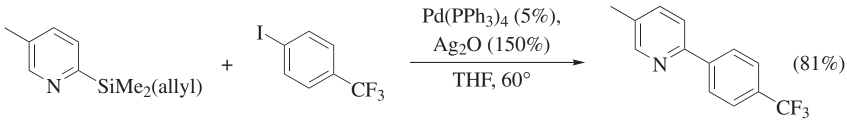
Aryl- and Heteroaryl-TGs. To enable the transfer of an aryl group, either two allyl groups[51] or three aryl groups[47] are needed. Only phenyl groups have served

as the transferable group thus far with aromatic bromides and chlorides (Eq. 42). A 2-pyridyl group requires only a single allyl group to transfer under activation by silver(I) oxide to aryl iodides (Eq. 43).[51]



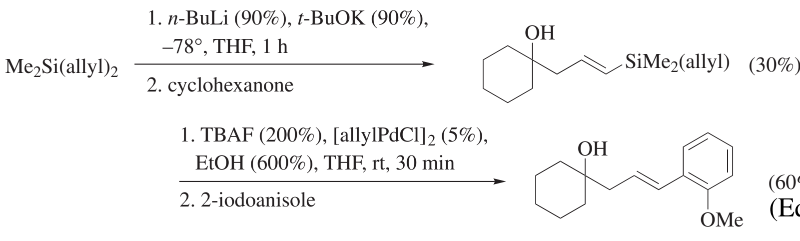
(Eq. 42)

X	Pd Source	Ligand	Solvent	Time (h)	
Cl	$[allylPdCl]_2$ (2.5%)	XPhos (10%)	THF/H_2O (25:1)	7	(95%)
Br	$PdCl_2$ (5%)	PCy_3 (10%)	$DMSO/H_2O$ (15:1)	12	(96%)



(Eq. 43)

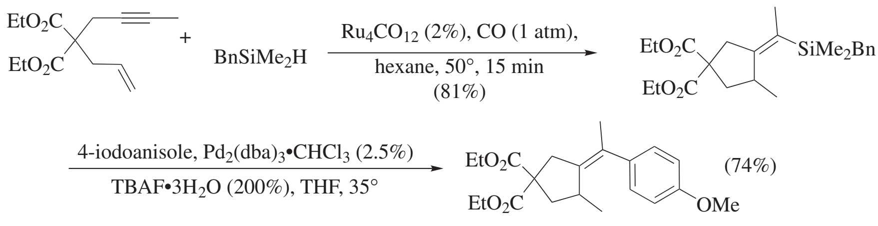
Alkenyl-TGs. Both allyl (or methallyl) and benzylsilanes serve as effective surrogates for silanols for the transfer of alkenyl groups. All of the allylsilanes are prepared by the addition of lithiated diallyl- or dimethallylsilanes to aldehydes or ketones. The resulting alkenylallylsilanes undergo facile cross-coupling with aryl iodides in the presence of TBAF (Eq. 44).[157]



(Eq. 44)

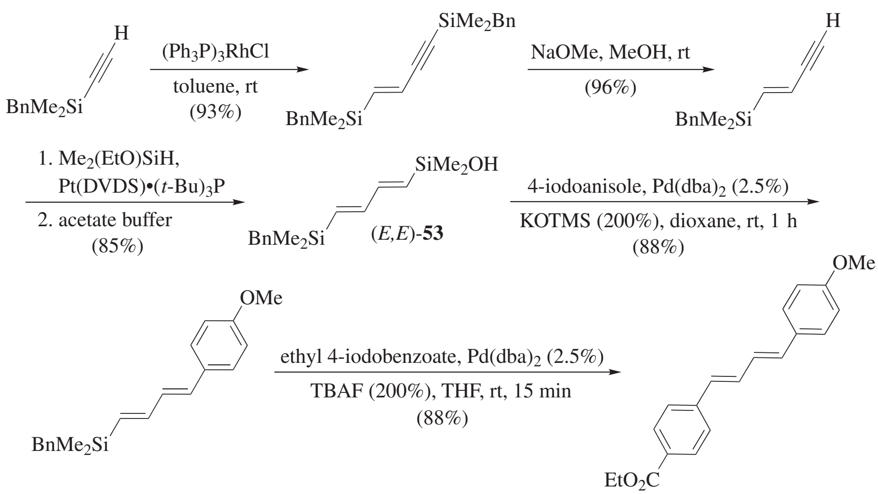
Benzylsilanes are much more versatile and have found application in sequential processes[158] that involve the introduction of the benzylsilane moiety by a number of different reactions, followed by a fluoride-promoted cross-coupling with aryl or alkenyl iodides. Transformations that have been employed to introduce the benzylsilane unit in a stereoselective fashion include hydrosilylation,[43,159] alkynylsilane dimerization,[44] silylcarbocyclization,[45] and silyl alkyne Alder-ene reaction.[43] The utility of benzylsilanes derives from their chemical stability and robustness as silanol surrogates for the transfer of stereodefined alkenyl groups. For example, benzyldimethylsilane effects a silylcarbocyclization under rhodium catalysis to create *exo* alkylidene silanes with perfect control of double bond

geometry. Fluoride-promoted cross-coupling proceeds in good yield with preservation of the double bond configuration to produce a tetrasubstituted *exo* alkylidene unit of defined geometry (Eq. 45).[45]



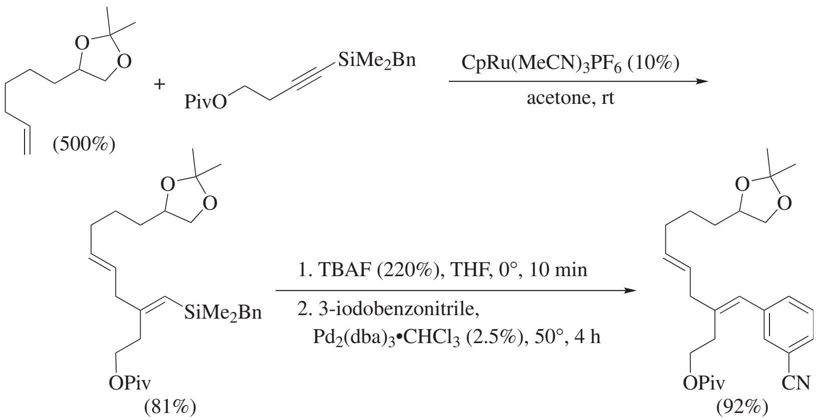
(Eq. 45)

The chemical stability and resistance of the benzyldimethylsilane unit to activation by mild Brønsted bases allows for the implementation of a bifunctional reagent that contains two different silyl groups capable of independent activation for cross-coupling. 1,3-Butadienyl-1,4-(bis)silane (E,E)-**53** (prepared by a three-step sequence) combines the potential for selective cross-coupling of the dimethylsilanol unit under activation by KOTMS, followed by cross-coupling of the benzyldimethylsilyl moiety under fluoride activation (Scheme 15).[44]



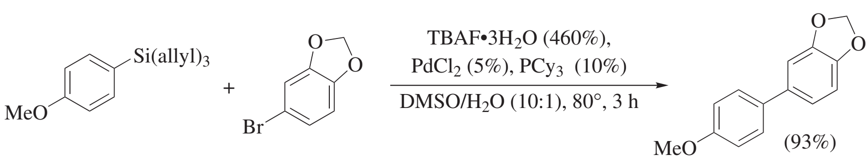
Scheme 15

Benzyldimethylsilanes are also easily incorporated into geometrically defined alkenes via an Alder-ene reaction with silylalkynes. Both the Alder-ene process and the subsequent fluoride-promoted cross-coupling can accommodate ester, ketone, carbonate, acetal, and cyano functional groups (Eq. 46).[43]

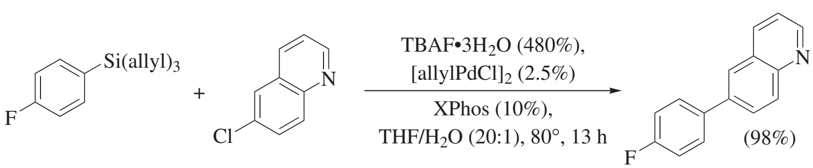


(Eq. 46)

Triallylsilanes. As was noted above, a stable precursor for efficient cross-coupling of aromatic transferable groups requires at least two labile groups on the silicon moiety. However, diallylsilanes present an ambiguity as to which of the remaining two groups will be transferred. Thus, the development of aryltriallylsilanes represents the logical extension of this concept.[46,47,160] Aryltriallylsilanes are prepared by the exhaustive allylation of aryltrichlorosilanes (prepared from the corresponding arylmagnesium halide and silicon tetrachloride) with allylmagnesium bromide. These silanes are resistant to the action of aqueous potassium hydroxide and potassium carbonate and undergo slow decomposition in aqueous HCl. However, they are also readily activated to cross-coupling in the presence of 4–5 equiv of TBAF in aqueous DMSO or aqueous THF. The scope of coupling partner is particularly broad in that aromatic iodides, bromides, and chlorides and heteroaromatic bromides and chlorides participate with assistance of the appropriate ligand, namely Cy_3P for bromides and XPhos[161] for chlorides (Eqs. 47, 48).



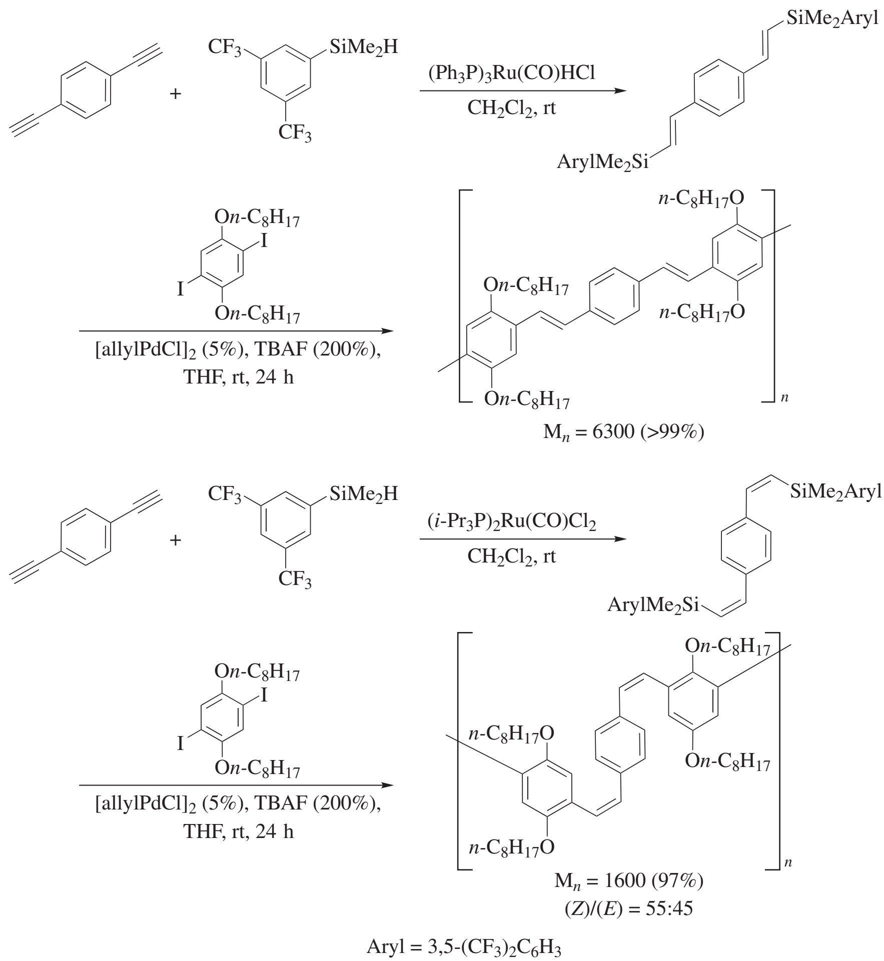
(Eq. 47)



(Eq. 48)

Arylalkylsilanes. *Alkenyl-TGs*. Because of the ambiguity of which substituent will be transferred, arylalkylsilanes have been used exclusively to activate alkenyl group transfers under both fluoride and alkoxide activation. The simple

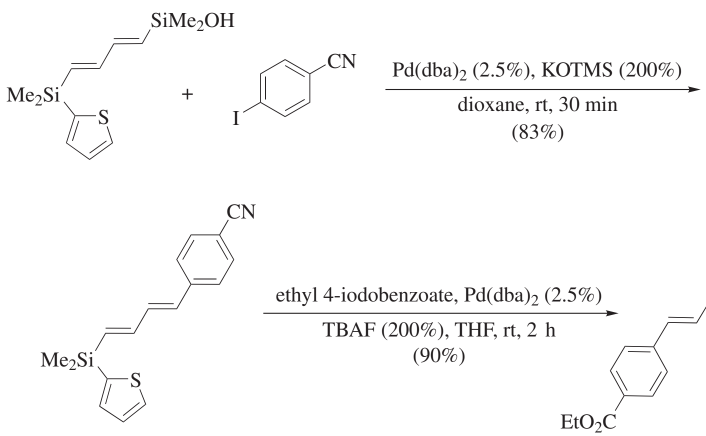
phenyldimethylsilyl group can facilitate the coupling of alkenes with aryl and heteroaryl iodides in the presence of TBAF.[162] Alternatively, the phenyl group can be cleaved in a separate step (with KOTMS and 18-crown-6) to the corresponding dimethylsilanol that undergoes coupling.[42] An early report of a *cine* substitution under these conditions has been corrected.[41] Under appropriate conditions, a diphenylmethylsilyl group can selectively transfer a 1-fluorovinyl moiety (instead of one of the phenyl groups) to aryl iodides in good yield.[163,164] Finally, the synthesis of stereodefined (*E*)- and (*Z*)-(polyphenylenevinylene)s can be achieved by the *syn* or *anti* selective hydrosilylation of 1,4-diethynylbenzene with 3,5-bis(trifluoromethyl)phenyldimethylsilane using different ruthenium catalysts. The fluoride-promoted cross-coupling of the (*E*)- and (*Z*)-styrylsilanes affords isomeric polymers (Scheme 16).[165–167]



Scheme 16

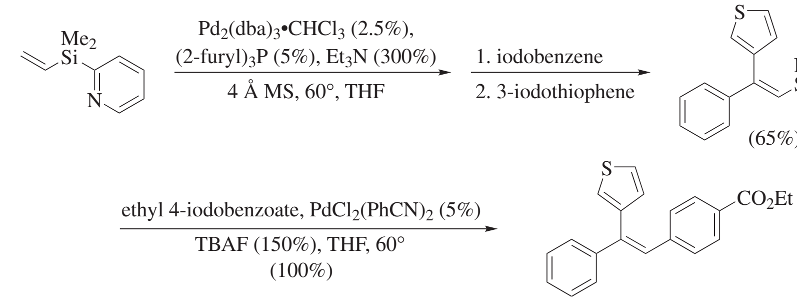
Heteroarylsilanes. The primary motivation for the development of this class of silafunctional groups is to provide easily handled silanes bearing a range of labile groups that can be removed under different conditions. Two heteroaryl groups, 2-pyridyl and 2-thienyl, have been extensively investigated in the context of alkenyl group transfers. A single example of a bis(2-furyl)silane has been reported for the transfer of an aryl group.[168]

Alkenyl-TGs. 2-Thienyldimethylsilyl groups are introduced onto alkenes by hydrosilylation with 2-thienyldimethylsilane. Both *syn* and *anti* hydrosilylation is achievable with judicious choice of catalyst.[49] The cross-coupling conditions are mild and no ligands are needed as the only coupling partners are aromatic iodides. 2-Thienyldimethylsilanes have found application in the synthesis of poly-4-phenylenevinylenes of different double bond configurations.[165] In addition, this activating group has served as a more labile silanol surrogate for two-directional functionalization of butadienes in cases where the benzyldimethylsilane leads to undesirable benzyl group migration instead of cross-coupling (Eq. 49).[44]

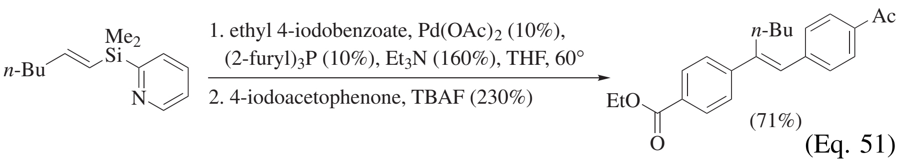


(Eq. 49)

The 2-pyridyldimethysilyl group has been introduced and extensively developed for the modular construction of polysubstituted alkenes.[52] The 2-pyridyl moiety provides two important features: (1) a powerful directing group for the selective introduction of carbon substituents onto alkynes or alkenes attached to the silicon atom, and (2) a labile function that is readily converted into a silanol for efficient cross-coupling. To date, only alkenyl TGs have been employed with this donor group. The directing ability of the 2-pyridyl group is illustrated in the elaboration of geometrically defined, polysubstituted alkenylsilanes by the sequential application of carbomagnesation or the Mizoroki-Heck reaction. This sequence can be carried out as individual steps (Eq. 50) or in a one-pot process (Eq 51).[169,170]



(Eq. 50)



(Eq. 51)

Through the agency of various combinations of directed Mizoroki-Heck coupling, protiodesilylation, and cross-coupling, a wide variety of polysubstituted alkenes can be constructed in geometrically defined form from various aryl halides (Figure 4).

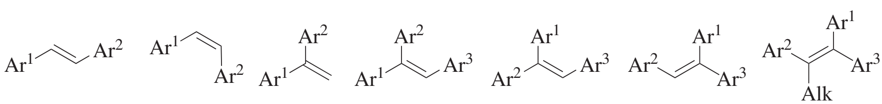
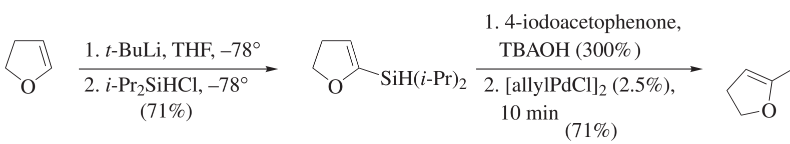


Figure 4. Permutations of products from sequential Mizoroki-Heck/cross-coupling.

Hydridosilanes. Hydridosilanes often serve as intermediates in the preparation of many chlorosilanes and silanols through a mild oxidation process. As such, their ability to serve as silanol surrogates directly in cross-coupling reactions was investigated in cases where the preparation of the silanol was problematic.[171] Silylation of 1-lithio vinyl ethers with diisopropylchlorosilane affords the stable, isolable hydridosilanes, which are converted in situ by treatment with TBAF or TBAOH (tetrabutylammonium hydroxide) into the corresponding silanol. The latter then undergoes efficient cross-coupling with aromatic iodides (Eq. 52).



(Eq. 52)

Cross-Coupling of Halosilanes

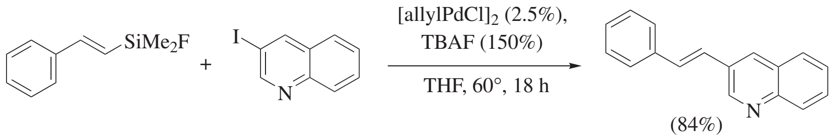
Halosilanes represent a large and highly diverse class of activating groups for silicon-based cross-coupling reactions. Early in the development of this process,

alkyl groups on triorganosilanes were systematically replaced with halogen atoms in an attempt to facilitate the formation of the hypercoordinate siliconate intermediate (with added fluoride) believed to be necessary for efficient transmetalation.[27] Both chloro- and fluorosilanes have been studied at all levels of substitution. Because the behavior of the coupling process depends primarily on the number rather than the identity of the halogen atoms, the organization will follow increasing heteroatom substitution.

Monohalosilanes

Monofluorosilanes. This class of activating substituents was among the first silafunctional groups to be investigated for their potential in cross-coupling reactions.[25,88,172] Fluorosilanes are readily prepared by treatment of chlorosilanes with copper(II) fluoride[173] or by protiodesilylation of allylic silanes with HF.[174]

Alkenyl-TGs. Monofluorosilanes are primarily used to activate the transfer of alkenyl groups. The reactions show good generality and excellent stereospecificity with respect to the substitution pattern on the transferable group. Aryl, heteroaryl, and alkenyl iodides serve as the electrophiles, and good stereospecificity is also seen in the electrophilic partner. All reported cross-couplings employ either TBAF or TASF as the fluoride activator (Eq. 53). A systematic study of the electronic effects of the electrophile on the constitutional site selectivity with (1-phenylethenyl)dimethylfluorosilane (**29**) was discussed above (Eq. 21).[89]



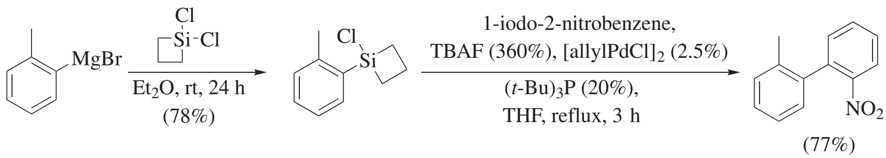
(Eq. 53)

A few examples of cross-coupling of alkenyl- and aryl monofluorosilanes with allylic carbonates and epoxides have been reported,[175,176] but these electrophiles cross-couple more effectively with difluorosilanes, which are presented in the next section.

Monochlorosilanes. This class of activating group has found only limited application in cross-coupling compared with the corresponding monofluorosilanes, probably because of the greater electrophilicity and hydrolytic stability of the latter.

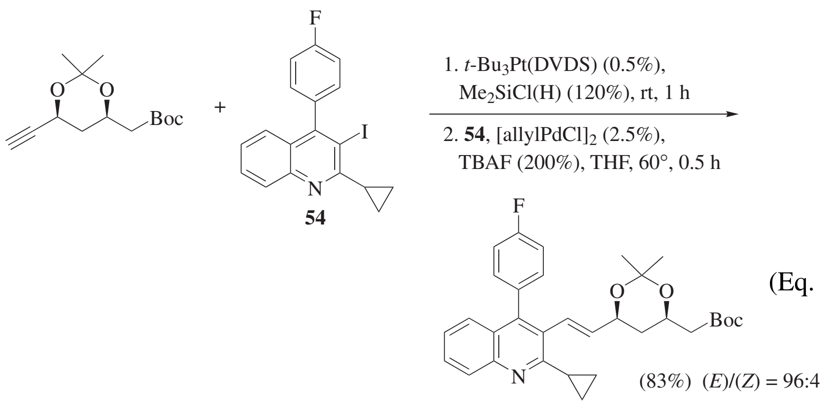
Aryl-TGs. The efficient transfer of aromatic groups generally requires more than one heteroatom substituent on silicon. This requirement is met by the use of chlorosilacyclobutanes, which are cleaved under the action of TBAF and provide biaryls with a range of aromatic iodides.[39] To suppress homocoupling, $(t\text{-Bu})_3P$ is

needed in significant amounts. The precursors are prepared by addition of the aryl-magnesium halide to commercially available dichlorosilacyclobutane (Eq. 54).



(Eq. 54)

Alkenyl-TGs. Only two reports of cross-coupling of chlorodimethylsilanes as activators of alkenyl groups are on record. In one report, simple vinyl- and (E)-styryl reagents are coupled with iodouracil derivatives.[88] In the second, the chlorosilane is generated in situ by hydrosilylation of an alkyne and then is coupled with 3-iodoquinoline **54** to prepare an HMG-CoA reductase inhibitor (Eq. 55).[177]



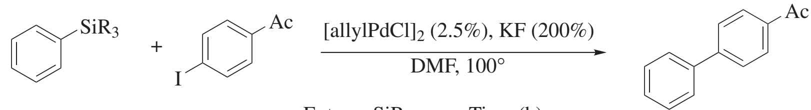
(Eq. 55)

A copper-catalyzed homocoupling of monochloro- and monofluorosilanes to transfer aryl, heteroaryl, alkenyl, and alkynyl groups is on record.[178]

Dihalosilanes

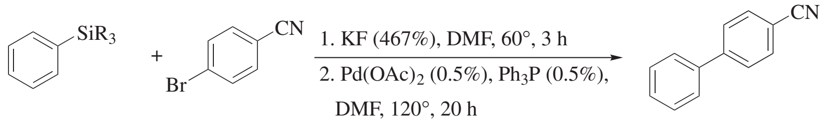
A systematic study of the structure of silafunctional donor groups clearly established the superiority of dihalosilanes to activate aromatic donor groups toward cross-coupling with aromatic halides.[73] By variation in the number of halogen substituents as well as the size of the spectator group, it was demonstrated that two fluorine atoms (Eq. 56, entries 3–5) and two chlorine atoms (Eq. 57, entries 2–4) provide the highest yields of biaryl products under a standard set of reaction conditions. In addition, the larger spectator group affords higher yields because the transfer of the alkyl is suppressed, or in the case of Ph_2SiCl_2 because

of statistics. However, this reagent is impractical because only one phenyl group is transferred.



Entry	SiR_3	Time (h)	
1	$SiMe_3$	24	(12%)
2	$SiMe_2F$	24	(15%)
3	$SiMeF_2$	12	(68%)
4	$SiEtF_2$	12	(71%)
5	$Si(n\text{-}Pr)F_2$	12	(87%)
6	SiF_3	10	(0%)

(Eq. 56)

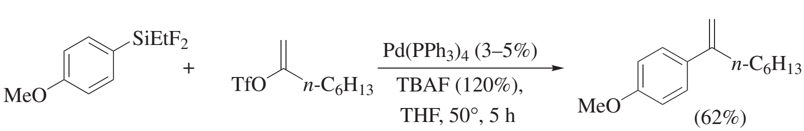


Entry	SiR_3	
1	$SiMe_2Cl$	(37%)
2	$SiMeCl_2$	(51%)
3	$SiEtCl_2$	(70%)
4	$SiPhCl_2$	(89%)
5	$SiCl_3$	(0%)

(Eq. 57)

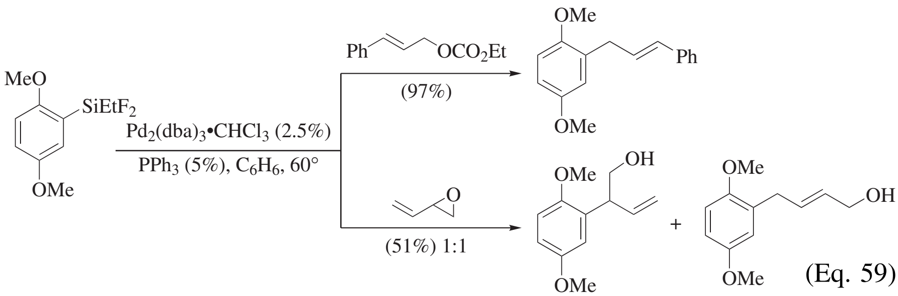
Difluorosilanes. Difluorosilanes are prepared from the corresponding dichlorosilanes by treatment with either antimony(III) fluoride or copper(II) fluoride.[179] The majority of the reported examples employ either ethyl- or *n*-propyldifluorosilanes. These reagents are stable in air.

Aryl- and Heteroaryl-TGs. The cross-coupling of aryldifluorosilanes with aryl iodides takes place under ligandless conditions using $[allylPdCl]_2$ as the catalyst and KF as the activator in either DMF or THF at elevated temperatures. The scope of aromatic donor groups is not large (only Me, OMe, and CF_3 substituents), but the scope of the functional groups on the electrophile is good (alcohol, ester, ketone, and aldehyde).[73,172,179,180] Aryl and alkenyl triflates also serve as electrophiles when $(Ph_3P)_4Pd$ and TBAF are used (Eq. 58).[181]



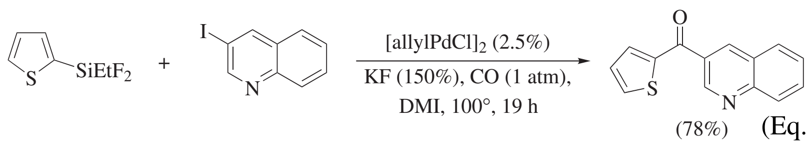
(Eq. 58)

Allylic epoxides and carbonates also serve as effective electrophiles; however, the site selectivity is good only for prenyl or cinnamyl substrates (Eq. 59).[175]

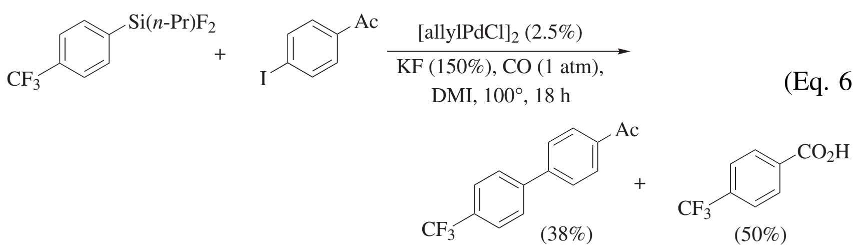


(Eq. 59)

A carbonylative cross-coupling has been developed for aryl- and heteroaryldifluorosilanes (Eq. 60).[179] The reaction requires only 1 atm of carbon monoxide, but if the aryl donor group is not reactive (i.e. electron deficient), then byproducts such as methyl ketones (from methyl group transfer) and carboxylic acids (from interception of the acylpalladium species by fluoride followed by hydrolysis) are observed (Eq. 61).[182]

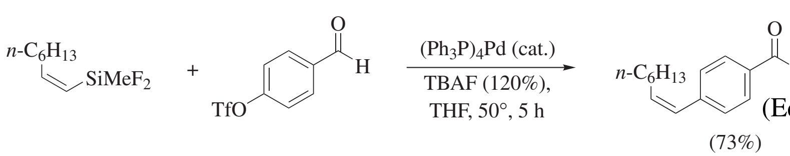


(Eq. 60)



(Eq. 61)

Alkenyl-TGs. Most of the characteristics of the cross-coupling of aryl- and heteroaryldifluorosilanes also apply to the cross-coupling of alkenyldifluorosilanes. Reactions with aryl iodides,[25,88] aryl and alkenyl triflates,[181] and allylic epoxides and carbonates[175,176] follow the same trends and in addition show high stereospecificity (Eq. 62).[181] However, the carbonylation reactions fail, giving mixtures of direct coupling and carboxylic acids along with the desired ketones.[179] This problem is ameliorated by the use of alkenyltrifluorosilanes, as described in a following section.



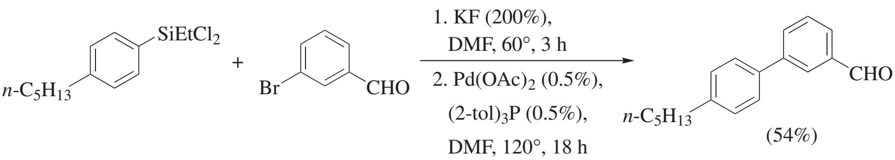
(Eq. 62)

Allyl-TGs. The only examples of cross-coupling of allylic difluorosilanes have been studied in the context of asymmetric induction with chiral substrates. Both *syn* and *anti* S_E2' pathways have been identified in the cross-coupling with 1-naphthyl triflate depending on the fluoride source (Scheme 8).[115]

Oxidative homocoupling of aryl-, heteroaryl-, and alkenyldifluorosilanes with copper(I) chloride in DMF has been described.[183]

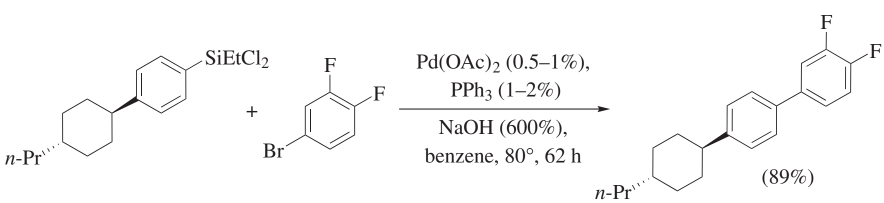
Dichlorosilanes. Insofar as dichlorosilanes are the precursors for the preparation of difluorosilanes, the ability to use the former reagents directly would have obvious benefits. However, the conditions developed for the cross-coupling of difluorosilanes do not lead to successful cross-coupling of dichlorosilanes.[184] Thus, a number of new conditions have been introduced.

Aryl and Heteroaryl-TGs. Three important modifications to the reaction conditions have allowed for the cross-coupling of aryldichlorosilanes with aromatic iodides, bromides, and chlorides. The most straightforward modification involves pretreatment of the dichlorosilane with KF in DMF at 60° for 3 h followed by addition of the palladium catalyst, a ligand if necessary, and the aryl bromide, and then heating the mixture to 120° (Eq. 63).[73] Although only a few different substituents have been introduced on the donor group, the functional group variation and compatibility on the electrophile is much wider (aldehyde, ketone, ester, nitrile, and nitro).



(Eq. 63)

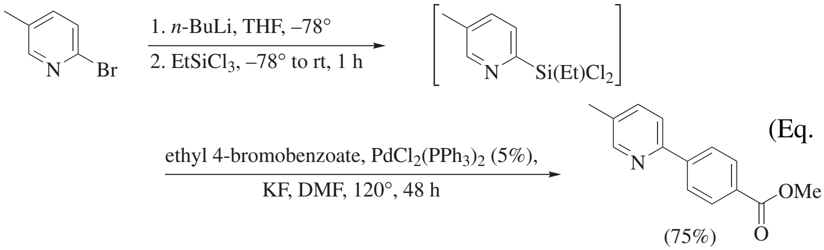
A second set of conditions applicable to both aromatic bromides and iodides involves the use of sodium hydroxide as the activator with either $Pd(OAc)_2$[185] or Pd/C[186] as the catalyst (Eq. 64).



(Eq. 64)

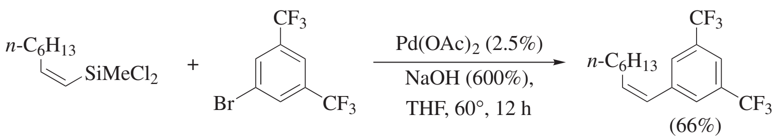
The most recent development allows the cross-coupling of aromatic chlorides.[187] This modification calls for the use of catalysts bearing strongly donating trialkylphosphines such as $(i\text{-Pr}_3P)_2PdCl_2$ or $(dcpe)_2PdCl_2$ in DMF at elevated temperature (120°) for 1–2 days.

2-Pyridyldichlorosilanes can be generated in situ and used directly for cross-coupling with a variety of aromatic bromides (Eq. 65).[30]

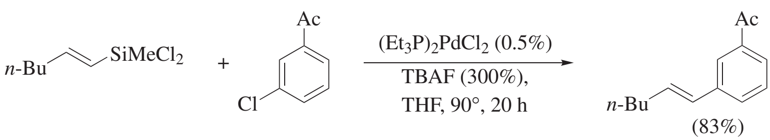


(Eq. 65)

Alkenyl-TGs. Alkenyldichlorosilanes undergo highly site-selective and stereospecific cross-coupling with aromatic bromides and chlorides and an alkenyl iodide.[185,187] Here again, two sets of conditions are available; activation with TBAF or with sodium hydroxide. Whereas no ligand is needed for the coupling with aromatic bromides with either activator, strongly donating trialkylphosphines such as those contained in $(i\text{-}Pr_3P)_2PdCl_2$ or $(Et_3P)_2PdCl_2$ are needed to effect cross-coupling of aromatic chlorides (Eqs. 66 and 67).



(Eq. 66)



(Eq. 67)

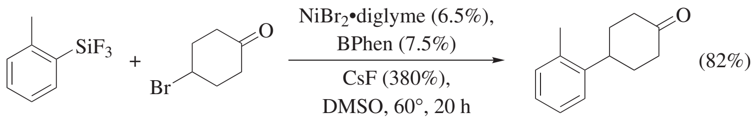
Trihalosilanes

Although the systematic studies of silafunctional groups shown in Eqs. 56 and 57 show that trihalosilanes are less reactive than the dihalosilanes under standard cross-coupling conditions, they have found utility in a number of specific applications. Only trifluorosilanes have been employed to date.

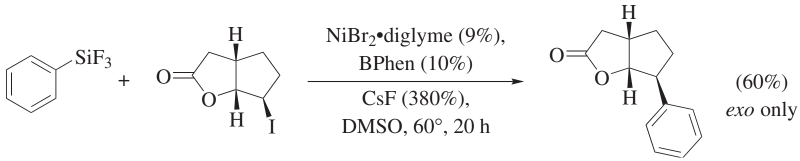
Trifluorosilanes. Trifluorosilanes are prepared from the corresponding trichlorosilanes by treatment with fluorosilicates.[188] These reagents are superior to antimony(III) fluoride and other metal fluorides because of their lower toxicity, cost, and milder reaction conditions.

Aryl-TGs. Aryltrifluorosilanes have found use as activated donors in nickel-catalyzed cross-coupling with aliphatic bromides.[189] This transformation takes place under mild conditions with cesium fluoride as the activator and with a wide range of primary and secondary bromides and iodides. Functional group compatibility on the electrophile is good (ketones, carbamates, lactones, acetals,

and cyano groups). The reaction is stereoconvergent (i.e. independent of halide configuration), which indicates the intermediacy of a radical or configurationally labile intermediate (Eqs. 68 and 69).[189]

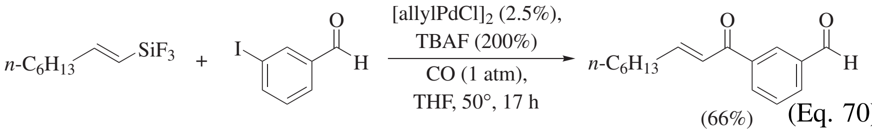


(Eq. 68)



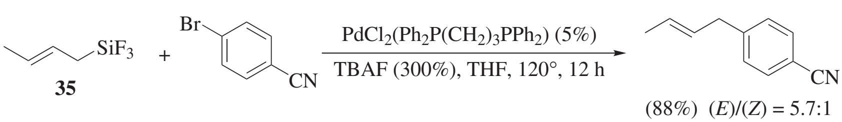
(Eq. 69)

Alkenyl-TGs. The sole application of alkenyltrifluorosilanes is for carbonylative coupling with aryl and alkenyl iodides. Mono- and difluorosilanes are not sufficiently activated for this process but good yields are obtained for (E)-1-octenyltrifluorosilane under 1 atm of carbon monoxide (Eq. 70).[179] Unfortunately, the reaction is not stereospecific as (Z)-1-octenyltrifluorosilane gives a mixture of (E) and (Z) isomeric products. A control experiment shows that the products isomerize under the cross-coupling conditions.

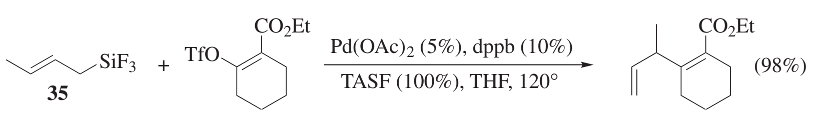


(Eq. 70)

Allyl-TGs. (E)-2-Butenyl-(**35**) and 3-methyl-2-butenyltrifluorosilane (**36**) undergo cross-coupling with aryl bromides, iodides, and triflates when activated by TBAF.[109] The site selectivity is dependent on the phosphine ligand (cf. Eqs. 23a, 23b) and the leaving group.[110] In general, for aryl halides a high γ-selectivity is obtained with Ph_3P, whereas high α-selectivity is obtained with dppp (Eq. 71). Curiously however, for enol triflates, dppb gives high γ-selectivity (Eq. 72).

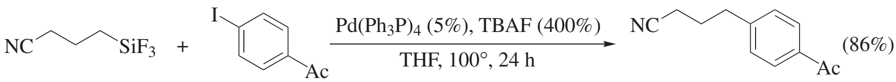


(Eq. 71)

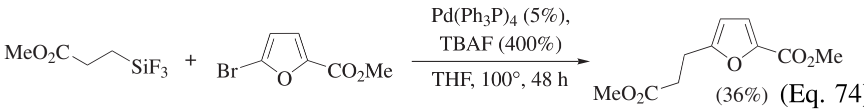


(Eq. 72)

Alkyl-TGs. The transfer of simple alkyl groups is rare for organosilicon-based cross-coupling reactions, but alkyltrifluorosilanes are capable of this transformation together with aryl bromides, iodides, and triflates. Only primary trifluorosilanes have been used thus far, although the functional group compatibility on the alkyl donor (cyano, ester, and ketone) and electrophile (aldehyde, ketone, nitro, and ester) is good (Eqs. 73 and 74).[190]



(Eq. 73)



(Eq. 74)

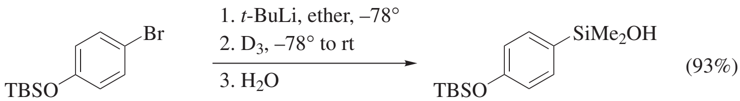
Cross-Coupling of Silanols and Silanolates

Organosilanols (and their conjugate bases) find ubiquitous application as stabilizing ligands in coordination chemistry of main group and transition metals complexes.[191] However, prior to 2000, the only applications of silanols in organic synthesis were the use of KOTMS for the mild saponification of methyl esters[192] and nitriles[193] and as an oxygen nucleophile in enantioselective allylic substitution.[194] In 2000, two independent reports demonstrated the utility of organosilanols as donors in cross-coupling reactions under activation by silver(I) oxide[37] or TBAF.[31] The advantages of organosilanols as coupling partners are manifold in comparison to the halosilanes, including: (1) ease of synthesis, (2) stability toward oxygen and moisture, (3) ease of purification, (4) chemical stability, and (5) diversity of synthetic methods for their preparation. An additional advantage of significant synthetic importance is the ability to activate the cross-coupling of organosilanols with Brønsted bases, thus avoiding the incompatibilities associated with fluoride. Moreover, the conjugate bases of organosilanols are stable, often free-flowing powders that are "self-activating" cross-coupling partners, i.e. require no additional activators. These two variants of cross-coupling are presented separately because of the differences in substrate scope. Even those cross-coupling reactions that undoubtedly involve the silanolate salt through in situ generation will be presented in the "Silanols" section, only those cross-couplings that employ the preformed, isolated silanolates are included in the subsequent section.

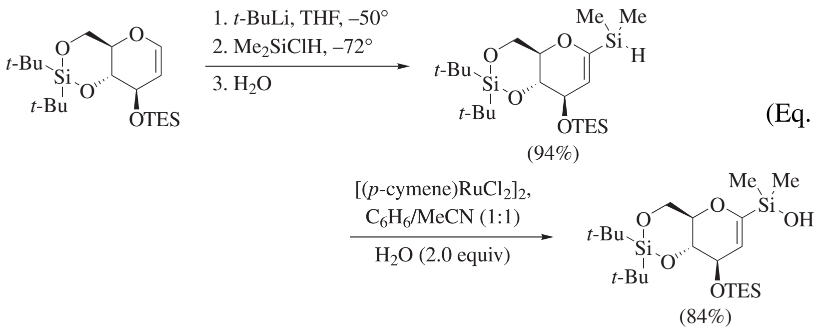
Silanols

Many different methods are available for the preparation of silanols and silanol surrogates from a variety of precursors. The most common method for introduction of a silanol unit involves the reaction of an organometallic reagent (lithium or magnesium) with a silicon electrophile. The most direct process involves the reaction of the organometallic reagent with hexamethylcyclotrisiloxane (D_3) (Eq. 75).[195] This method works well for aryl- and alkenyllithium reagents. Less

reactive organometallic species or those unstable at higher temperatures require more reactive silicon electrophiles such as dimethyldichlorosilane or dimethylchlorosilane. Whereas the former can be converted into the corresponding silanol by mild hydrolysis (acetate buffer), the latter is converted to the silanol by oxidation with water or an alcohol under catalysis by ruthenium or iridium complexes (Eq. 76).[196]



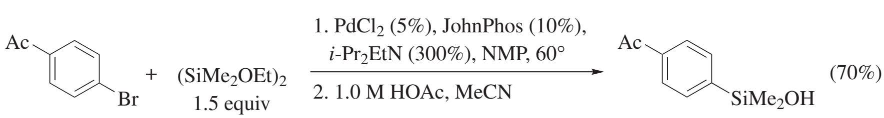
(Eq. 75)



(Eq. 76)

Hydrosilylation of alkynes is a powerful method for creating carbon-silicon bonds with site and stereoselectivity. For this method, silanol surrogates are needed and can be found in the many commercially available hydrosilanes bearing chloro, alkoxy, or silyloxy substituents. More robust surrogates such as benzylsilanes are also available. The steric course of the hydrosilylation is dependent on the transition-metal catalyst: (1) platinum catalysts (e.g., H_2PtCl_6, (DVDS)Pt•(t-Bu_3P))[197] react with terminal alkynes to give (E)-1-alkenylsilanes via a *syn* process whereas $[(C_6H_6)RuCl_2]_2$ promotes an *anti* addition process to afford (Z)-alkenylsilanes.[198] Remarkably, the cationic ruthenium complex $[(Cp)Ru(MeCN)_3]^+ PF_6^-$ reacts with terminal alkynes to afford 2-alkenylsilanes.[159]

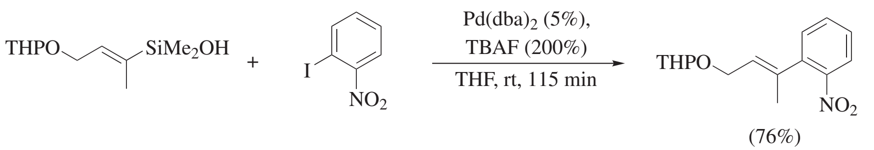
A palladium-catalyzed insertion method has been developed to allow the introduction of silanols on cyclic substrates wherein formation of an organometallic reagent is precluded by sensitive functionality (Eq. 77).[199] For effective reaction with aryl bromides, a bulky electron-rich phosphine (JohnPhos)[200] is required. The pH of the workup is critical to suppress formation of the disiloxane.



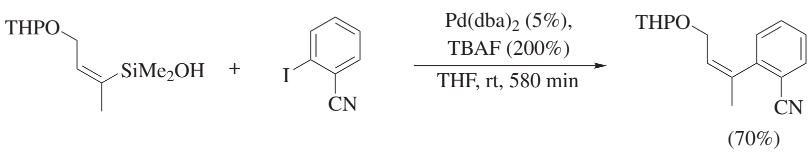
(Eq. 77)

Fluoride Activation. *Aryl-TGs*. Only a simple phenyl group has been transferred under these conditions by the use of phenyldimethylsilanol in combination with a limited number of aryl iodides. A stoichiometric amount of silver(I) oxide is also used together with TBAT.[201]

Alkenyl-TGs. This class represents a very large number of examples that employ acyclic and cyclic alkenylsilanes of varying substitution patterns in cross-coupling with aryl, heteroaryl, and alkenyl halides. The stereospecificity of cross-coupling of simple alkenylsilanes has been discussed previously (Eq. 7) and is further illustrated for a prenylating agent (Eqs. 78a, 78b).[79] For the iodide electrophiles, no phosphine ligand is needed and the reactions take place at room temperature with electron-deficient, electron-rich, and sterically hindered arenes. In a competition study, dimethyl-, diethyl-, diisopropyl-, and diphenylsilanols react at approximately the same rate under activation by TBAF.[72]



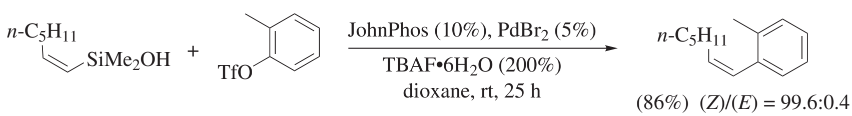
(Eq. 78a)



(Eq. 78b)

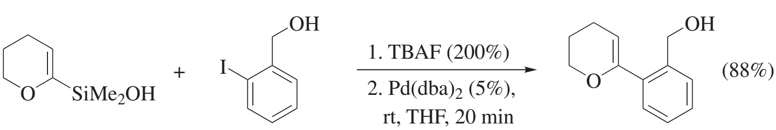
Cross-coupling reactions with alkenyl iodides and bromides proceed with high geometrical selectivity and only minor amounts of *cine* substitution products (Eq. 19).[31,79,171] Diisopropylsilanols give slightly higher geometrical selectivities compared to dimethylsilanols.[31]

Aryl triflates can participate in cross-coupling reactions but the conditions need to be carefully adjusted. To facilitate the oxidative addition step, an electron-rich, hindered phosphine (JohnPhos) is needed and to suppress fluoride-assisted S–O bond cleavage of the triflate, the TBAF is hydrated with 6 to 8 equiv of water (Eq. 79).[202] For electron-deficient aryl triflates, TBAF•30H_2O is needed.



(Eq. 79)

α-Alkoxyalkenylsilanols, both cyclic (pyranyl and furanyl) and acyclic, undergo ready cross-coupling with aryl iodides under the standard conditions with TBAF (Eq. 80).



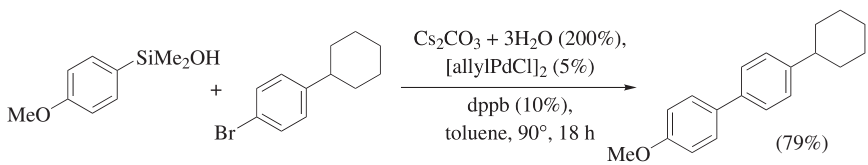
(Eq. 80)

Alkynyl-TGs. A limited set of simple alkynylsilanols undergo a "copper-free," Sonogashira-type cross-coupling with aryl iodides using $(Ph_3P)_4Pd$ and TBAF.[138] In this case, the silanol offers no advantage when compared to the scope of fluoride-promoted coupling of alkynyltrimethylsilanes (Eqs. 31–36).

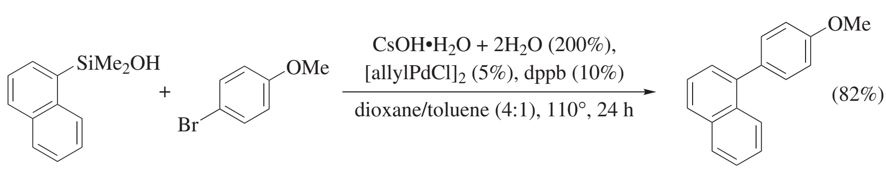
Brønsted Base Activation. For this disparate collection of cross-coupling reaction conditions, the only unifying characteristic is that the activators are all Brønsted bases. Thus, under this rubric is found activation by silver(I) oxide, potassium trimethylsilanolate, cesium carbonate, cesium hydroxide, potassium *tert*-butoxide, and sodium hydride. Undoubtedly, the corresponding silanolate is being formed to some extent and is likely the active component. However, because the parent silanol is the species employed in these processes, these conditions are described in this section.

Aryl-TGs. The first reported use of silanols in a cross-coupling reaction employed a full equivalent of silver(I) oxide as the activator in the presence of $Pd(OAc)_2$ in warm THF.[36,37,203] Phenylsilanols bearing electron-donating and withdrawing groups can be used with similarly modified aryl iodides. It is likely that silver activates the arylpalladium iodide by abstraction of an iodide to form a cationic palladium(II) species and activates the arylsilanol through formation of a hypercoordinate complex. The intermediacy of a palladium(II) silanolate was not suggested.

Phenylsilanols can also undergo cross-coupling in the presence of cesium bases (carbonate or hydroxide). However, the bases must carry 2–3 molecules of water of hydration to reverse the formation of inactive disiloxanes formed from the silanols under the elevated temperatures needed to effect cross-coupling with aryl iodides and bromides (90–110°).[204,205] In addition, ligands play an important role in suppressing the formation of homocoupling products from, as well as reduction of, the electrophile (Eqs. 81, 82). The failure of disiloxanes to undergo cross-coupling under Brønsted base activation sharply contrasts with their behavior under fluoride activation, which supports the divergence of mechanism under the different reaction conditions (Schemes 4 and 5). The limited scope of arylsilanol TGs and harsh reaction conditions limit the utility of this method, which has been replaced by the use of the preformed potassium silanolate salts (vide infra).

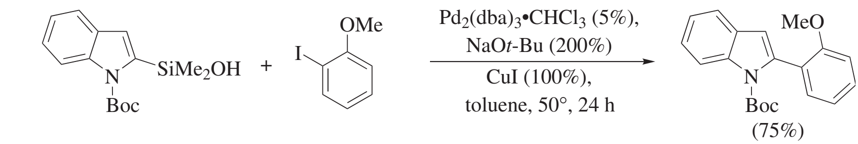


(Eq. 81)

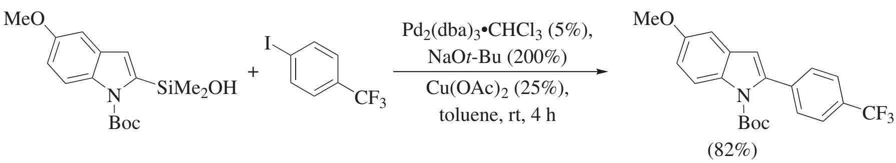


(Eq. 82)

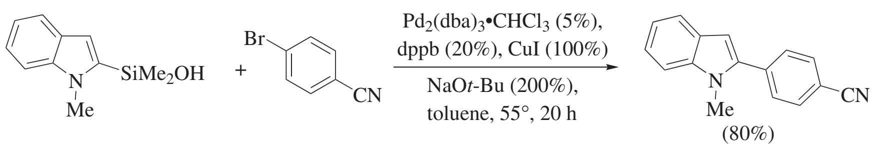
Heteroaryl-TGs. A significant number of π-excessive heteroaromatic silanols have been prepared and three different conditions for their cross-coupling reactions have been developed, two of which involve the use of the parent silanol.[206–208] *N*-Boc- and *N*-methyl 2-indolyldimethylsilanol undergo smooth cross-coupling with aryl bromides and iodides in the presence of sodium *tert*-butoxide and 1.0 equiv of copper(I) iodide to suppress protiodesilylation (Eqs. 83–85). The amount of copper can be reduced to 25 mol % with activated indole derivatives.



(Eq. 83)

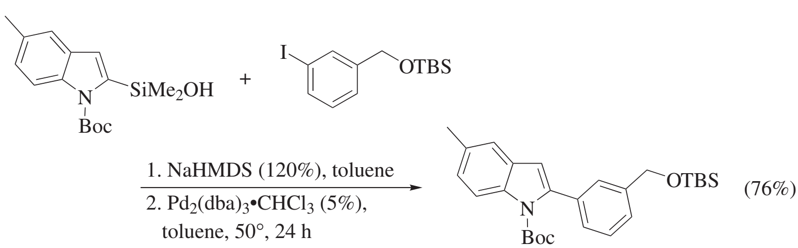


(Eq. 84)

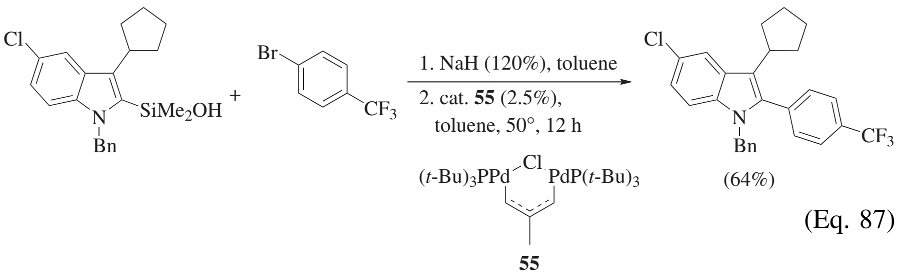


(Eq. 85)

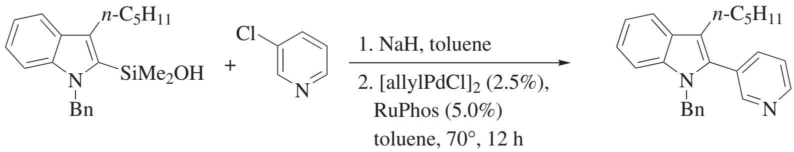
A more general protocol involves the stoichiometric deprotonation of the heteroarylsilanol with either sodium hydride or sodium hexamethyldisilazide. This modification allows a number of important advances, including the elimination of copper(I) salts to suppress protiodesilylation (no protons) and the ability to cross-couple with aryl and heteroaryl bromides and chlorides (Eqs. 86–88).[208,209] For the less reactive electrophiles, an appropriate phosphine ligand or precatalyst is needed to effect oxidative addition. SPhos,[210] RuPhos,[211] and the palladium(I) dimer **55**[212] serve in this capacity.



(Eq. 86)

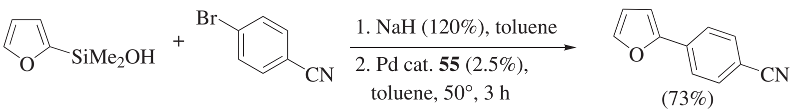


(Eq. 87)



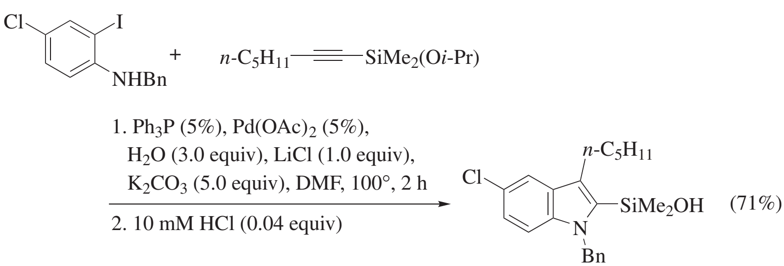
(Eq. 88)

In addition, 2-furyl-, 2-thienyl-, and *N*-Boc-(2-pyrrolyl)dimethylsilanols undergo cross-coupling under these conditions with a similar scope of electrophile (Eq. 89).[208]



(Eq. 89)

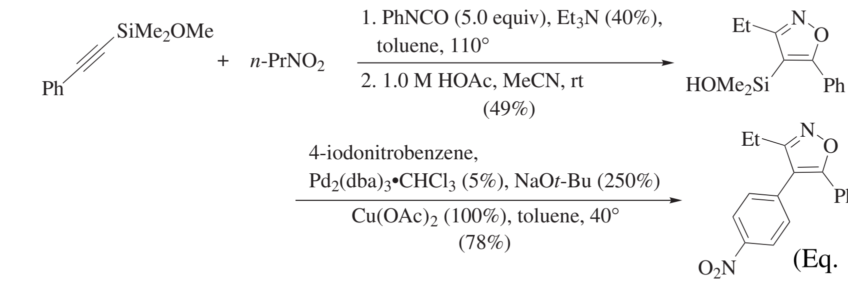
The 3-substituted-2-indolylsilanols in Eqs. 86−88 are prepared by a variant of the Larock indole synthesis that employs alkynylsilyl ethers and places the silanol group in the 2-position for coupling (Eq. 90).[209] 2−Iodo-*N*-alkyl anilines are used as precursors with both isopropyl and *tert*-butylsilyl ethers. These silyl ethers are sufficiently robust to withstand the Larock heteroannulation conditions and can be deprotected with very mild acid hydrolysis. The sequence then allows for the controlled construction of 2,3-disubstituted indoles from anilines whereby unsymmetrical alkynes would otherwise lead to mixtures of constitutional isomers. The cross-coupling of isolated, preformed sodium silanolate salts represent the third variant, which is discussed in the next section.



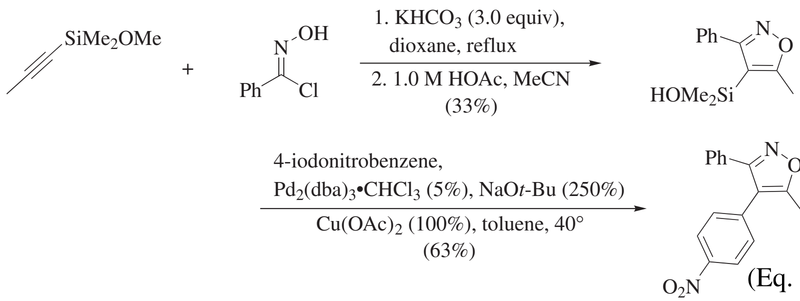
(Eq. 90)

Another sequential process that first constructs a silylated heterocycle, which is then used for cross-coupling, involves the [3+2] cycloaddition of nitrile oxides with alkynylsilyl ethers (Eqs. 91a, 91b).[213] The nitrile oxides can be generated

under two different conditions, both sufficiently mild to allow the use of an alkynylsilyl methyl ether as the 2π-component. The [3+2] cycloaddition reactions proceed in modest regioselectivity (ca. 4–5:1), and the minor constitutional isomers can be removed easily. The cross-coupling reactions require extensive optimization to suppress protiodesilylation. As had been observed before, copper salts, this time copper(II) acetate, are used to maximize the yield of the cross-coupling product.

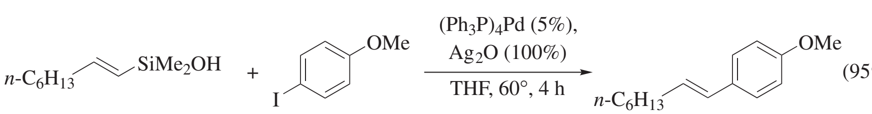


(Eq. 91a)

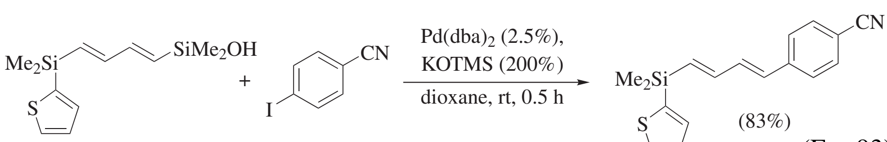


(Eq. 91b)

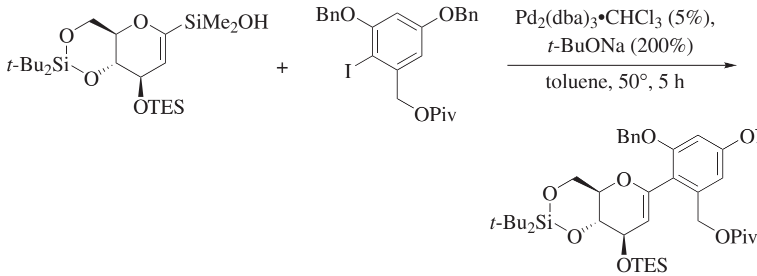
Alkenyl-TGs. Several different methods of activation have been employed for this family of organosilanols including silver(I) oxide[37] (Eq. 92), KOTMS[32,44] (Eq. 93), sodium *tert*-butoxide[214,215] (Eq. 94), and potassium hydride[216] (Eq. 95). Both aromatic and olefinic iodides are active partners. Functional group compatibility is good and the reactions are stereospecific with respect to the alkenylsilanol unit. Diisopropylsilanols react significantly slower (ca. 20-fold) than dimethylsilanols under activation by KOTMS.



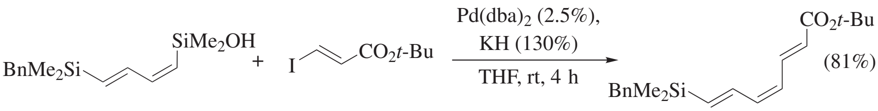
(Eq. 92)



(Eq. 93)

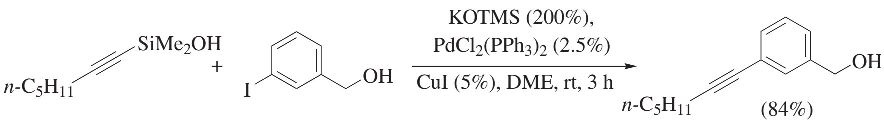


(Eq. 94)



(Eq. 95)

Alkynyl-TGs. As is the case with trimethylsilylalkynes, the silanol version of the Sonogashira reaction offers little advantage under activation by fluoride, but activation by KOTMS leads to a significantly more rapid transmetalation (room temperature compared to 65–120°). Copper(I) iodide is essential for clean cross-coupling, and in this report the substrates are limited to aryl iodides (Eq. 96).[217]



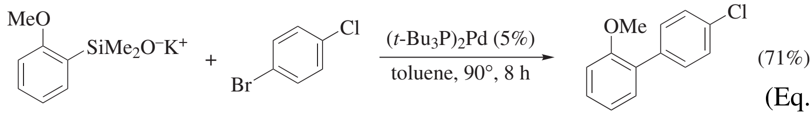
(Eq. 96)

Silanolates

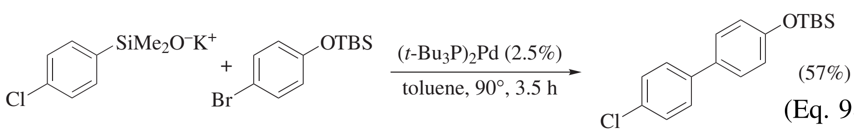
Although silanolate salts are certainly the reactive species in the cross-coupling reactions carried out under Brønsted base activation, these salts are always generated in situ from the parent silanol. Depending on the strength of the Brønsted base employed, the formation of the silanolate may or may not be quantitative. Moreover, the conjugate acid remains in the reaction mixture (except in the case of NaH and KH). The preformation and isolation of the sodium or potassium silanolates (from the corresponding hydrides) offers a number of preparative advantages. First, silanols dimerize to the corresponding disiloxanes in the presence of acids or bases, and isolating the metal salt prevents this process. Second, using the isolated preformed silanolate in the reaction not only simplifies the experimental procedure (adding one reagent as opposed to the silanol and base), but also ensures that the cross-coupling partner is always present in its active form. Moreover, a metal silanolate can be generated cleanly with a stoichiometric quantity of metal hydride, without the need for an excess of an activator. The use of an excess of the activator can be problematic in the cross-coupling reaction for several reasons. Surplus activator (i.e. KO*t*-Bu, KOTMS) can compete with silanolate for the Pd center of the arylpalladium halide. As a competitive inhibitor, the activator can form an inactive species in the cross-coupling reaction where it serves as a ligand on the Pd(II) aryl complex. This process sequesters palladium in an inactive form, and subsequently slows the cross-coupling reaction.[77]

Silanolate must displace the activator to allow the Pd to reenter the catalytic cycle as the palladium silanolate. An excess of the activator can also limit functional group compatibility. For example, when NaO*t*-Bu is employed with substrates bearing ethyl esters, a competing transesterification reaction takes place.[54] Furthermore, excess amounts of hydride reagents give reduction products,[32] and are incompatible with substrates bearing sensitive functional groups. The direct introduction of the silanolate avoids these problems and many of these salts are stable, free-flowing powders.

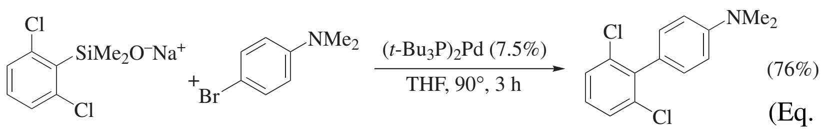
Aryl-TGs. The limitations encountered in the cross-coupling of arylsilanols under Brønsted base activation (Eqs. 81, 82) are substantially overcome by the use of potassium arylsilanolate salts in combination with $(t\text{-Bu}_3\text{P})_2\text{Pd}$.[54] A wide range of arylsilanolates bearing various functional groups (alkoxy, dialkylamino, trifluoromethyl, fluoro, chloro, and alkoxycarbonyl) couple effectively with aryl bromides and chlorides bearing an equally diverse set of functional groups (halo, alkoxy, silyloxy, and alkoxycarbonyl) in good yield. In addition, various heteroaromatic bromides function as cross-coupling partners (Eqs. 97–101).[54] Other ligand/catalyst combinations show more limited generality.[218]



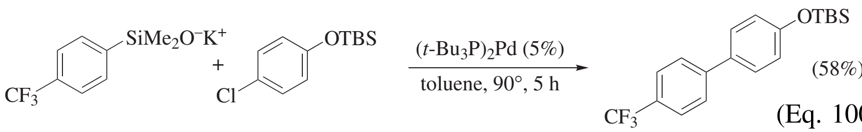
(Eq. 97)



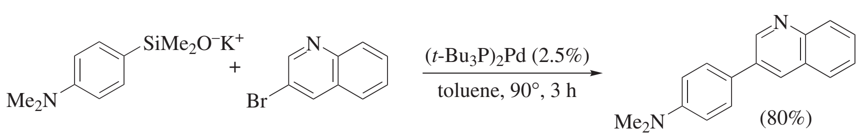
(Eq. 98)



(Eq. 99)



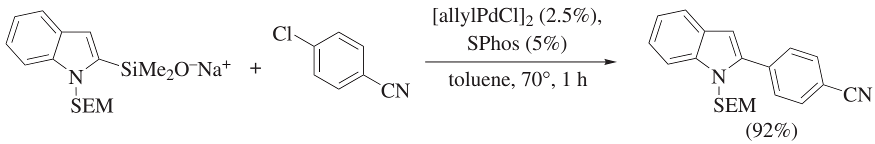
(Eq. 100)



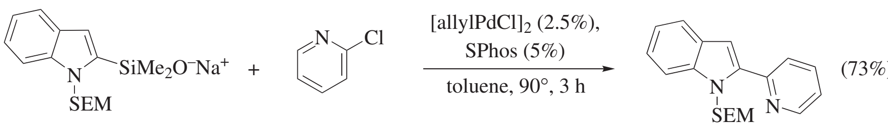
(Eq. 101)

Heteroaryl-TGs. The successful cross-coupling of in situ generated sodium silanolates of π-excessive heterocyclic silanols illustrated in Eqs. 83–89 can be

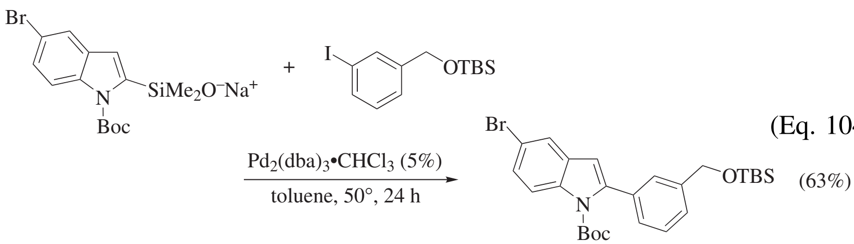
extended to other heterocycles and coupling partners by the use of preformed salts. For example, the preformed *N*-SEM-2-indolylsilanolate can engage in cross-coupling with a variety of aryl and heteroaryl bromides and chlorides whereas the 5-bromo-*N*-Boc-2-indolylsilanolate couples with iodides selectively,[208] and *N*-Me-3-pentyl-2-indolylsilanolate (formed by a Larock annulation process)[209] couples cleanly with a variety of aryl bromides. Moreover, a large number of 2-benzofuranylsilanolates undergo smooth coupling under similar conditions (Eqs. 102–107).[54]



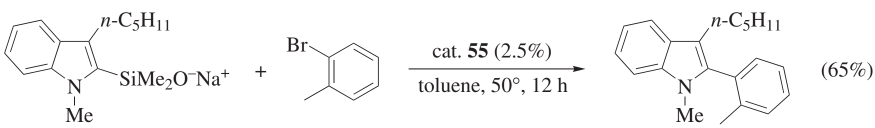
(Eq. 102)



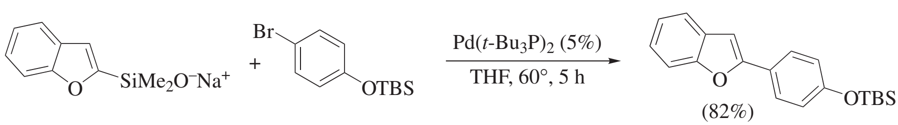
(Eq. 103)



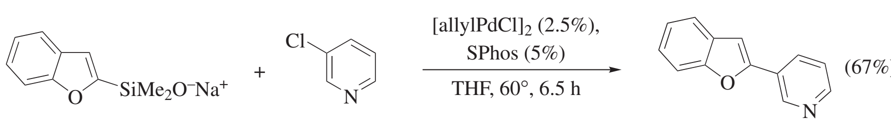
(Eq. 104)



(Eq. 105)

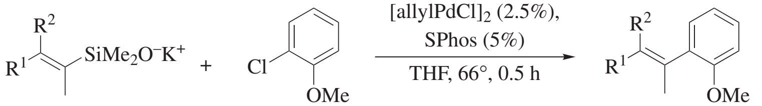


(Eq. 106)



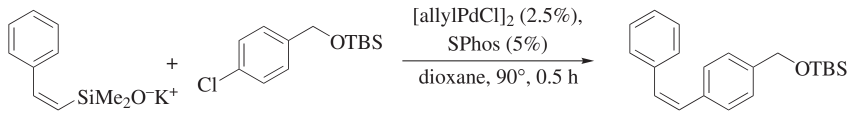
(Eq. 107)

Alkenyl-TGs. Although alkenylsilanols undergo efficient cross-coupling by various methods of activation with Brønsted bases, the preformed potassium salts are highly effective in reactions with aromatic and heteroaromatic chlorides.[80] These reactions display superior generality with respect to the acceptor, extremely high stereospecificity for a number of different alkenylsilanolate substitution patterns, and overall higher yields than the couplings with the corresponding bromides or iodides (Eqs. 108–110).[80] The absence of byproducts derived from reduction or homocoupling of the electrophile accounts for the better performance of these reactions.



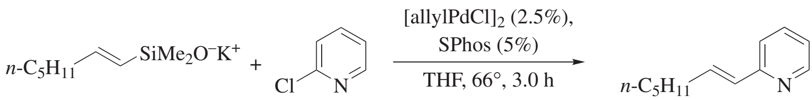
R^1	R^2	(E)/(Z)		(E)/(Z)
Et	H	98.9:1.1	(97%)	98.8:1.2
H	Et	98.6:1.4	(89%)	98.6:1.4
Me	Et	>99.5:0.5	(95%)	99.5:0.5

(Eq. 108)



(97%) (Z)/(E) = 99.5:0.5

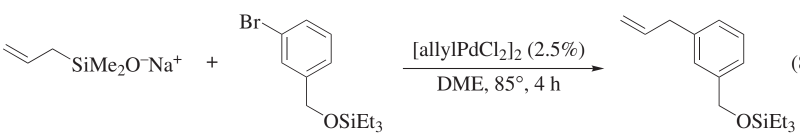
(Eq. 109)



(87%) (E)/(Z) = 99.6:0.4

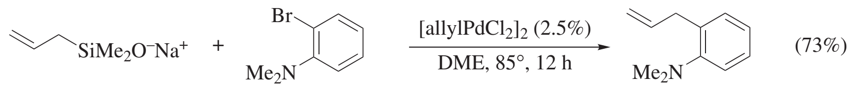
(Eq. 110)

Allyl-TGs. The sodium salts of allyldimethylsilanol and 2-butenyldimethylsilanol undergo palladium-catalyzed cross-coupling with a wide variety of aryl bromides to afford allylated and crotylated arenes.[108] The reaction of the allyldimethylsilanolate affords good yields of the allylation products from both electron-rich and sterically hindered bromides (Eqs. 111, 112). Sodium 2-butenyldimethylsilanolate ((*E*)/(*Z*) = 80:20) affords good yields of the γ-substituted product with electron-rich and electron-poor bromides (Eqs. 113–115). The site selectivity (Eq. 24) is strongly influenced by olefinic ligands (dibenzylideneacetone and norbornadiene). Configurationally homogeneous (*E*)-silanolates give slightly higher γ-selectivity than the pure (*Z*)-silanolates.

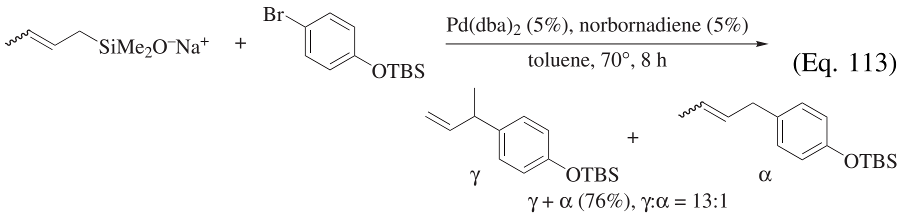


(86%)

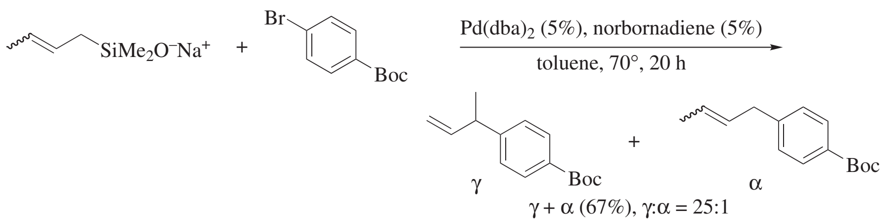
(Eq. 111)



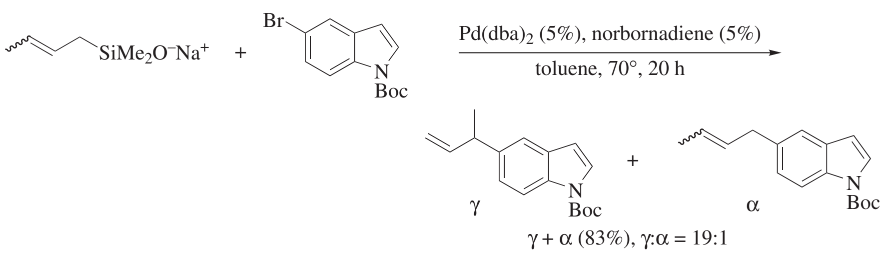
(Eq. 112)



(Eq. 113)



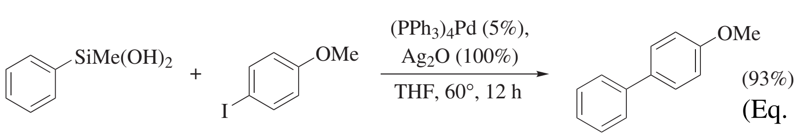
(Eq. 114)



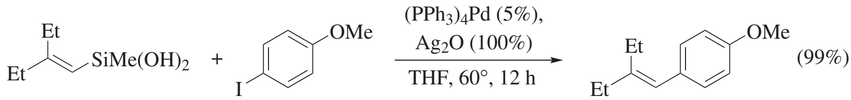
(Eq. 115)

Silanediols and -Triols

Aryl- and Alkenyl-TG's. Both aromatic and olefinic silanediols and -triols can be prepared by buffered hydrolysis of the corresponding chlorides and react with aromatic iodides under standard cross-coupling conditions.[37] In general, silanediols react more readily than the corresponding silanols and afford comparable or higher yields (Eqs. 116 and 117). In some cases, the crude hydrolysis product can be used directly in the cross-coupling reaction without isolation of the silanediol.



(Eq. 116)



(Eq. 117)

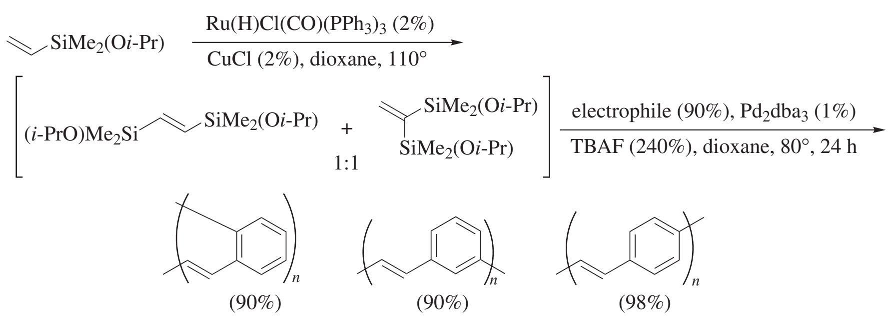
Cross-Coupling of Monoalkoxysilanes

This family of monofunctional cross-coupling precursors is distinguished by the diversity of synthetic methods that have been applied to the introduction of the silyl moiety into the substrates. These transformations allow a logical classification into reactions that create acyclic silyl ethers and cyclic silyl ethers as described below. The vast majority of cross-coupling reactions of alkoxysilanes involve alkenyl transferable groups by virtue of the methods for their construction and subsequent intended application. All cross-couplings are promoted by fluoride.

Acyclic Silyl Ethers

Three principal methods have been employed for preparing silyl ethers for cross-coupling: (1) ruthenium-catalyzed silylative coupling, (2) addition of lithioallylsilanes to carbonyl compounds, and (3) silylstannylation or hydrosilylation.

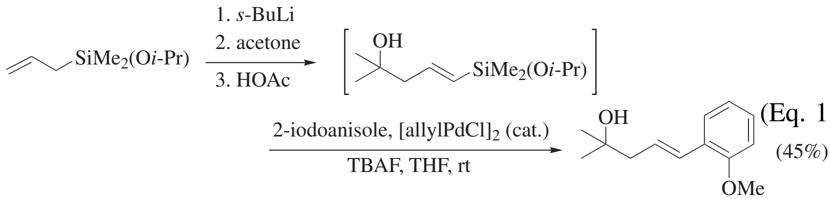
Ruthenium-Catalyzed Silylative Coupling. In a process that superficially resembles cross-metathesis, vinylsilanes undergo a mechanistically distinct cross-metathesis or dimerization with loss of ethylene to form higher alkenylsilanes or 1,2-disilylethenes.[219−221] The specific application that involves monoalkoxysilanes is the ruthenium-catalyzed dimerization of isopropoxydimethylvinylsilane to produce a mixture of 1,1- and 1,2-disilylethenes, which are employed as a mixture for the synthesis of arenevinylene polymers (Scheme 17).[104] Polymers derived from 1,2-, 1,3-, and 1,4-diiodobenzene as well as 2,5-diiodothiophene have been prepared.



Scheme 17

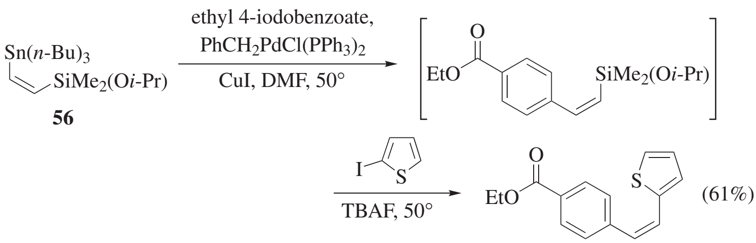
Addition of Lithioallylsilane. Lithiation of isopropoxydimethylallylsilane with s-BuLi in THF followed by addition of the anion to aldehydes and ketones results in the exclusive formation of the γ-addition product bearing an (E)

double bond. These alkenylsilanes (often not isolated) undergo fluoride-promoted cross-coupling under standard conditions with aryl iodides (Eq. 118).[157,222] The alkoxysilane is most likely converted into a silanol under the coupling conditions.[74]



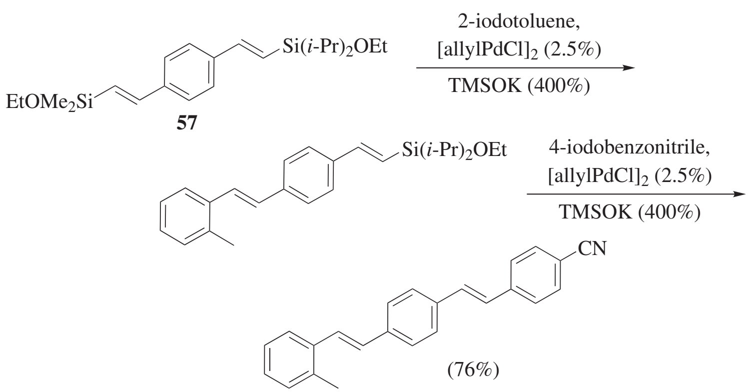
(Eq. 118)

Silylstannylation and Hydrosilylation. A useful linchpin reagent, **56**, is prepared by the *syn* silylstannylation of acetylene in high yield. This reagent allows for the stepwise installation of aryl residues toward the synthesis of unsymmetrical stilbenes (Eq. 119).[128]



(Eq. 119)

The bis(alkenylsilylether) **57** is prepared by a combination of platinum-catalyzed hydrosilylation and ruthenium-catalyzed silylative coupling (Eq. 120). Selective cross-coupling of **57** is made possible by the large difference in the reactivity of the diisopropylsilyl ether vs. the dimethylsilyl ether under activation by KOTMS.[72]



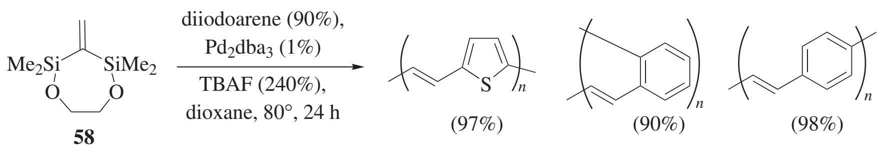
(Eq. 120)

Cyclic Silyl Ethers

Four principal methods have been employed for preparing cyclic silyl ethers for cross-coupling: (1) ruthenium-catalyzed silylative coupling,

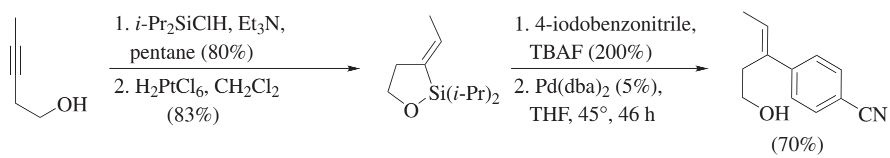
(2) intramolecular hydrosilylation, (3) intramolecular silylformylation, and (4) ring-closing metathesis.

Ruthenium-Catalyzed Silylative Coupling. Cyclic (bis)silylethene **58** is prepared by ruthenium-catalyzed silylative coupling of 1,2-bis(dimethylvinysilyl-oxy)-ethane. Remarkably, this reagent undergoes cross-coupling with diiodo-arenes exclusively via a *cine* substitution pathway to afford poly(arenevinylene)s in high yield (Eq. 121).



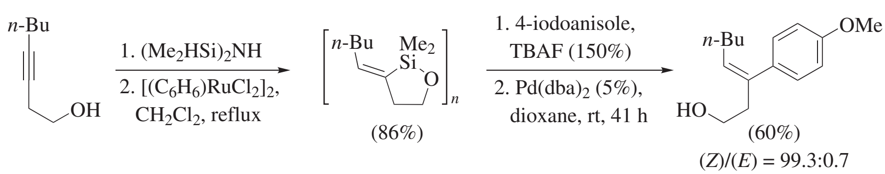
(Eq. 121)

Intramolecular Hydrosilylation. Platinum-catalyzed intramolecular hydro-silylation is a powerful method for the construction of cyclic silyl ethers.[223] Five-membered ring siloxanes can be prepared in good yield starting from stable diisopropyl silyl ethers. The use of Speier's catalyst affords the (E)-*exo*-alkylidene double bond with high geometrical selectivity resulting from *syn* addition. Cross-coupling with aryl iodides under standard conditions with TBAF affords geometrically defined homoallylic alcohols in good yield (Eq. 122).[224] This transformation can also be run as a one-pot process starting from the homo-propargyl alcohol by in situ silylation with tetramethyldisilazane followed by the same sequence as above.[26] Overall yields are generally higher in the one-pot process.



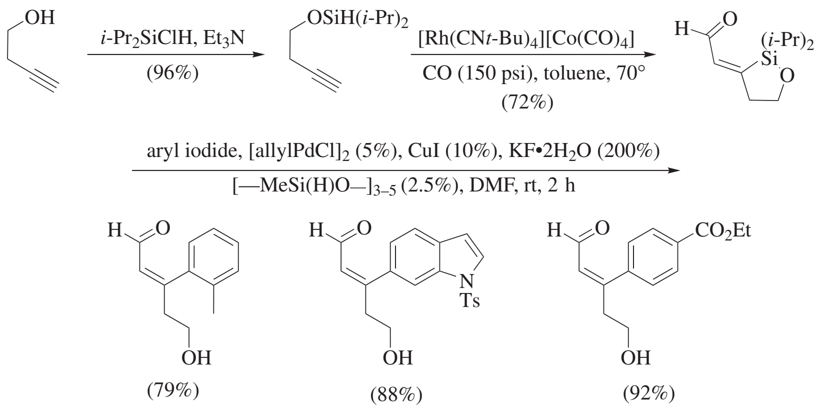
(Eq. 122)

Intramolecular hydrosilylation using a ruthenium catalyst affords the isomeric (Z)-*exo*-alkylidene siloxanes via an *anti* addition. However, because of the additional steric encumbrance, only dimethylsilyl ethers are sufficiently reactive. These ethers are difficult to isolate because of rapid oligomerization, but can be prepared in situ and used efficiently in subsequent cross-couplings (Eq. 123).[198]



(Eq. 123)

Intramolecular Silylformylation. The intramolecular hydrosilylation process can be run under an atmosphere of carbon monoxide (150 psi) to afford products of *syn* addition of a formyl group and the siloxane tether. The formyl group renders these alkenylsilanes considerably less reactive and an extensive optimization of fluoride source, palladium catalyst, solvent, and additives is required to suppress protiodesilylation. Satisfactory reaction conditions for cross-coupling with a range of aromatic iodides could be identified (Scheme 18).[81] The diverse functionality in these products is noteworthy.

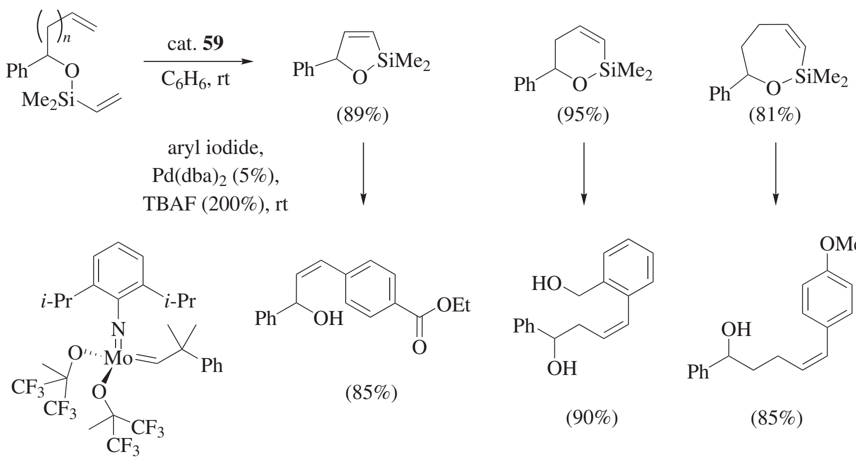


Scheme 18

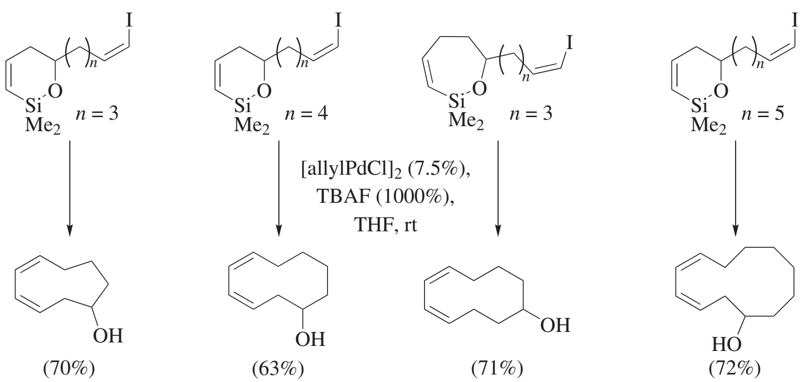
Ring-Closing Metathesis. This process is used to form cyclic siloxanes containing an endocyclic double bond as part of the alkenylsilane. Subsequent cross-coupling of the alkenylsiloxane can be performed either inter- or intramolecularly.

Tandem Ring-Closing Metathesis/Intermolecular Cross-Coupling. Whereas ring-closing metathesis with allylsilanes is facile, reaction with vinylsilanes is very sluggish, likely because of steric effects. Thus, the more reactive molybdenum-based catalysts such as **59** are required to effect the closure of vinyldimethylsilyl ethers of unsaturated alcohols (Scheme 19). Five-, six-, and seven-membered siloxane rings can be formed by this process and all three substrates undergo facile cross-coupling with aryl iodides under standard conditions with TBAF.[225,226] The endocyclic double bond assures the stereospecific construction of (Z)-unsaturated alcohols.

Tandem Ring-Closing Metathesis/Intramolecular Cross-Coupling. A useful modification of the tandem process involves the attachment of the organic electrophile to the constructed siloxane. The subsequent intramolecular cross-coupling reaction affords medium-sized rings bearing a (Z,Z)-1,3-diene unit. Adjusting the length of the chain that links the two alkenes in the substrate allows control of the ring size and position of the hydroxy group in the product (Scheme 20). In this way, nine-, ten-, eleven- and twelve-membered rings can be prepared, although high dilution (slow addition) reaction conditions are necessary to achieve good



Scheme 19



Scheme 20

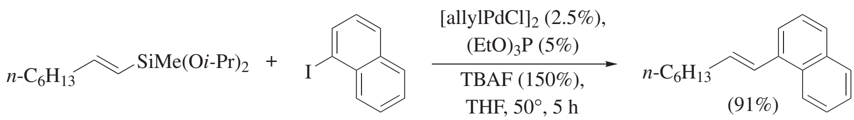
yields of monomeric products.[226,227] Medium-ring ethers can also be prepared by this process.[228,229]

Cross-Coupling of Di- and Trialkoxysilanes, and Silatranes

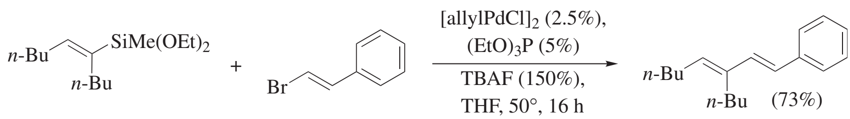
Dialkoxysilanes

Alkenyl-TGs

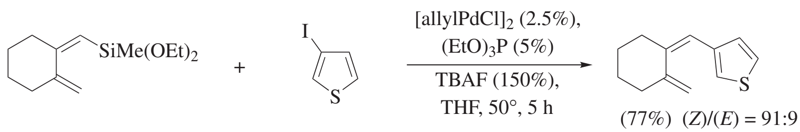
Only two reports describe the cross-coupling of dialkoxysilanes, both of which employ hydrosilylation of alkynes to introduce the silyl moiety. In one study, all three families, mono-, di- and trialkoxyalkenylsilanes, undergo cross-coupling under activation by TBAF and all three reacted, although the mono- and dialkoxysilanes give higher yields. Cross-coupling with aryl iodides as well as alkenyl iodides and bromides are successful (Eqs. 124–126).[26,230]



(Eq. 124)



(Eq. 125)



(Eq. 126)

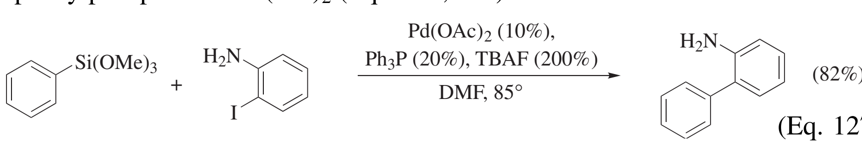
Trialkoxysilanes

This family of organosilicon donors is among the most commonly employed cross-coupling reagents. Although comparative studies of di- and trialkoxyalkenylsilanes show the former to be more reactive,[26] such direct comparisons are not available for the corresponding arylsilanes.[231] More likely, the prevailing reason for the use of trialkoxyarylsilanes is the commercial availability of a few simple derivatives that dominate the application with a wide variety of electrophiles. Accordingly, the following sections are organized according to the electrophilic partner, the leaving group, and the mode of activation. The vast majority of the donors are trimethoxy- or triethoxysilanes with a few examples of tris(2,2,2-trifluoroethoxy)silanes.[70]

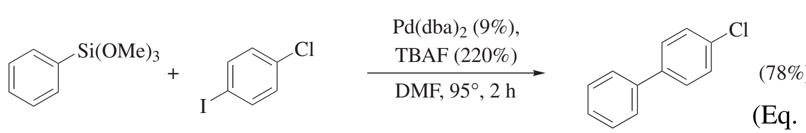
Aryl-TGs

This donor family represents the largest class of coupling partners although the structural diversity of the substrates is not large, for the most part, substituted benzenes and naphthalenes.

Aryl Iodides. *Fluoride Activation*. Aryl iodides bearing amino (alkylamino), acetamido, nitro, alkoxy, and chloro groups undergo cross-coupling under standard conditions with TBAF activation using either palladium acetate/triphenylphosphine or $Pd(dba)_2$ (Eqs. 127, 128).[70,232]



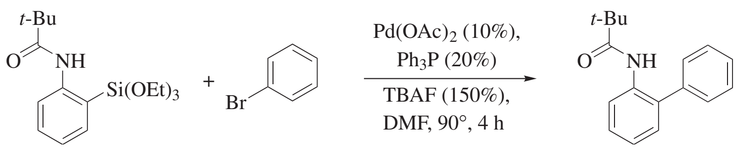
(Eq. 127)



(Eq. 128)

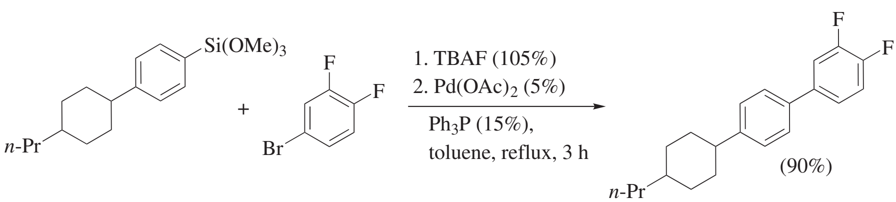
Non-Fluoride Activation. Catalysis of organic reactions by transition-metal nanoparticles has become a viable synthetic method with many practical advantages.[233] Only a few simple examples of coupling of aryltrimethoxsilanes with aryl iodides are known but they still represent a novel technology. The catalytic system involves formation of nanoparticles from sodium chloropalladate in NaOH solution in the presence of sodium dodecylsulfate (SDS) at 100°.[234]

Aryl Bromides. *Fluoride Activation.* A much greater diversity of aryltrialkoxysilanes has been introduced for the cross-coupling with aryl bromides. The parent phenyltrimethoxysilane undergoes high yielding cross-coupling reactions with a wide variety of aromatic bromides (bearing amino, nitro, alkoxy, keto, or trifluoromethyl substituents) under the same conditions employed for aromatic iodides.[70,232,235,236] In addition, $PdCl_2$ can be used as the catalyst[237] and a thiourea-based ligand has also been employed.[238] Functionalized aryltrialkoxysilanes bearing various *ortho* (carbamate, amide, alkoxy, methoxymethyl) and *para* substituents undergo cross-coupling under standard conditions (Eq. 129, 130).[239,240] These partners can be prepared by directed ortho-metalation and trapping with various silicon electrophiles, whereas *para*-substituted aryltrialkoxysilanes are prepared by treatment of aryllithium reagents with $Si(OEt)_4$. In addition, bis(2-diisopropylphosphinophenyl) ether (**60**) provides high yields for cross-coupling of both electron-rich and electron-deficient aryltrimethyoxysilanes (Eq. 131).[241]

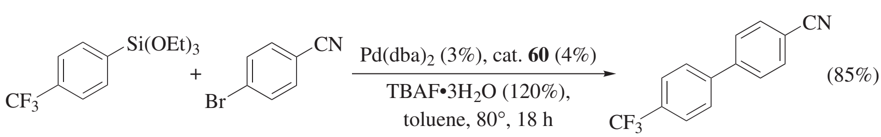


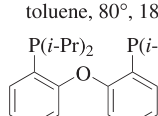
(86%)

(Eq. 129)



(Eq. 130)

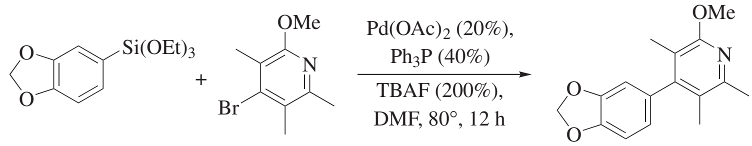




60

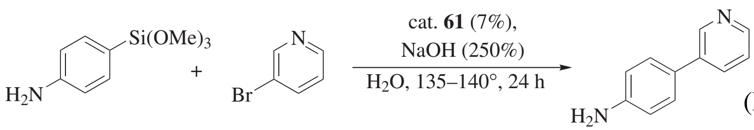
(Eq. 131)

A number of heteroaromatic bromides, primarily pyridines and thiophenes, also undergo smooth cross-coupling under standard reaction conditions (Eq. 132).[236,237,240–244]

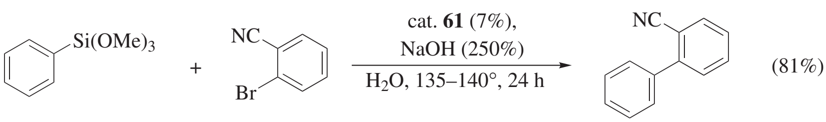


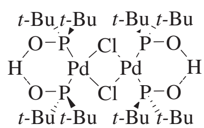
(Eq. 132)

Non-Fluoride Activation. In addition to palladium nanoparticles that have been applied in catalytic reactions with aromatic bromides to a greater extent than with aromatic iodides,[234] a catalytic system has been reported based on the dimeric palladium(II) phosphinous acid complex **61** that operates in hot (140°) aqueous NaOH. A wide range of aromatic and heteroaromatic bromides undergo high-yielding cross-coupling reactions (Eqs. 133a and 134b).[245]



(Eq. 133a)

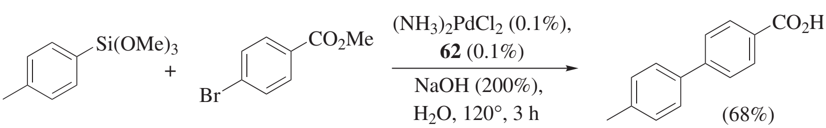


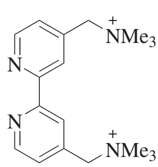


61

(Eq. 133b)

A second catalytic system has been developed that employs a water-soluble bipyridine ligand **62** in aqueous NaOH (Eq. 134).[246] Palladium loadings are low (0.1–0.01 mol%) and the diversity of cross-coupling partners is good, but reaction conditions are far from mild.





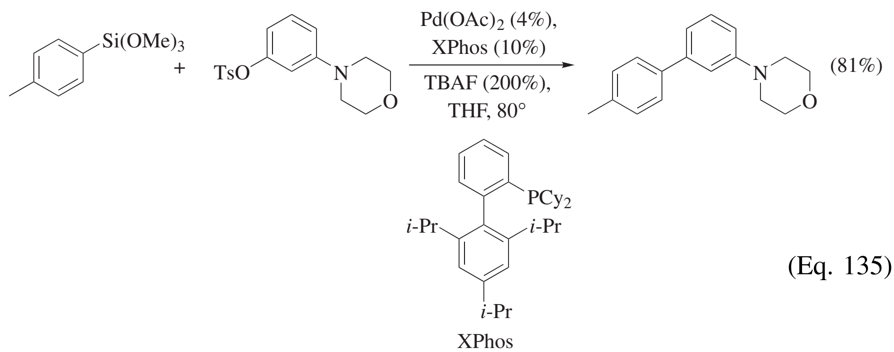
62

(Eq. 134)

Aryl Chlorides. *Fluoride Activation.* As with all other donors, the ability to engage aromatic chlorides in cross-coupling reactions depends on the choice of ligand to facilitate oxidative addition. For phenyltrimethoxysilane as well, bulky, electron-rich phosphorus-based ligands are used such as **60**,[241] **61**,[247] and 2-(dicyclohexylphosphino)biphenyl[236] (Cyclohexyl JohnPhos) together with simple aromatic chlorides. Other than the choice of ligand, the cross-coupling reactions are unexceptional in that either palladium acetate or $Pd(dba)_2$ is used as the catalyst together with TBAF.

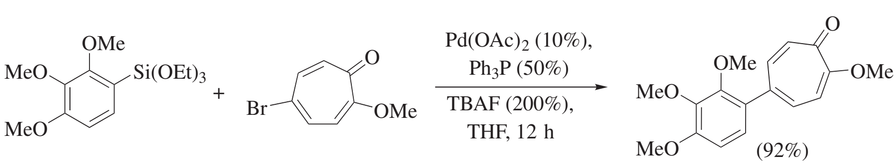
Non-Fluoride Activation. The large majority of the reported reactions for cross-coupling with aromatic and heteroaromatic chlorides employ phenyltrimethoxysilane under the same conditions described for the coupling of aromatic bromides above, namely aqueous NaOH with $Pd(OAc)_2$/thiourea ligand,[238] $(NH_3)_2PdCl_2$/bipyridyl ligand **62**,[246] or palladium complex **61**.[245]

Aryl Sulfonates. Both aryl mesylates[248] and aryl tosylates[249] undergo cross-coupling with aryltrimethoxysilanes under standard conditions (palladium acetate, TBAF, THF/*t*-BuOH) in the presence of XPhos[250] as the critical ligand additive. The structural diversity explored in the aryl sulfonate and the aryl siliconate is modest (Eq. 135).

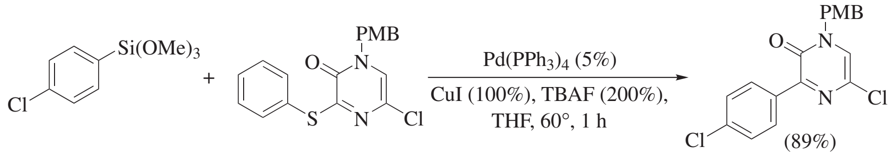


(Eq. 135)

Alkenyl Electrophiles. A limited number of alkenyl bromides and thio ethers have been successfully cross-coupled with aryltrimethoxysilanes under fluoride activation. The bromides react under standard conditions (Eq. 136)[251] whereas the thio ethers (more accurately heterocyclic thio ethers) require the addition of copper(I) iodide in stoichiometric quantities to couple cleanly (Eq. 137).[252]



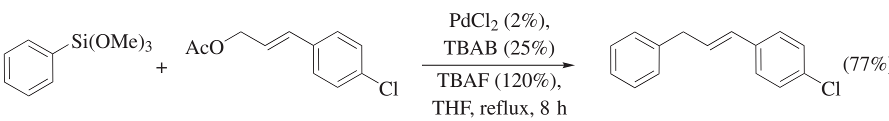
(Eq. 136)



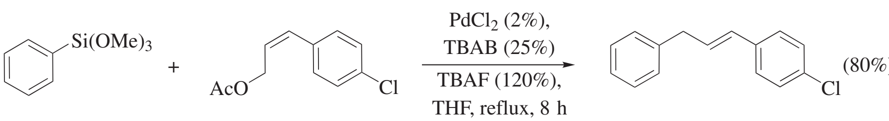
(Eq. 137)

Allylic Carboxylates. Arylation of allylic benzoates and acetates can be effected by cross-coupling with aryltrimethoxysilanes under fluoride activation. The primary issues in this transformation are the site selectivity on the allyl moiety and configuration of the resulting double bond. For acyclic allylic electrophiles, both of these issues are relevant whereas for cyclic allylic electrophiles the double bond is necessarily *cis*.

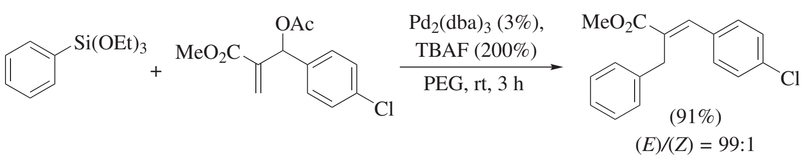
Acyclic Electrophiles. Arylation of linear allylic benzoates and acetates gives rise to linear products in a stereoconvergent fashion (Eqs. 138a, 138b)[253,254] whereas branched electrophiles afford either linear or branched products depending on the substitution pattern of the allylic group. If the terminus of the branched allylic electrophile is unsubstituted, then linear products are obtained with high (E)-selectivity (Eq. 139). However, branched products are formed when the alkene is contained in a ring (Eq. 140).[255]



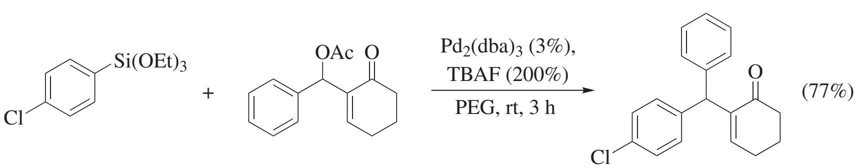
(Eq. 138a)



(Eq. 138b)

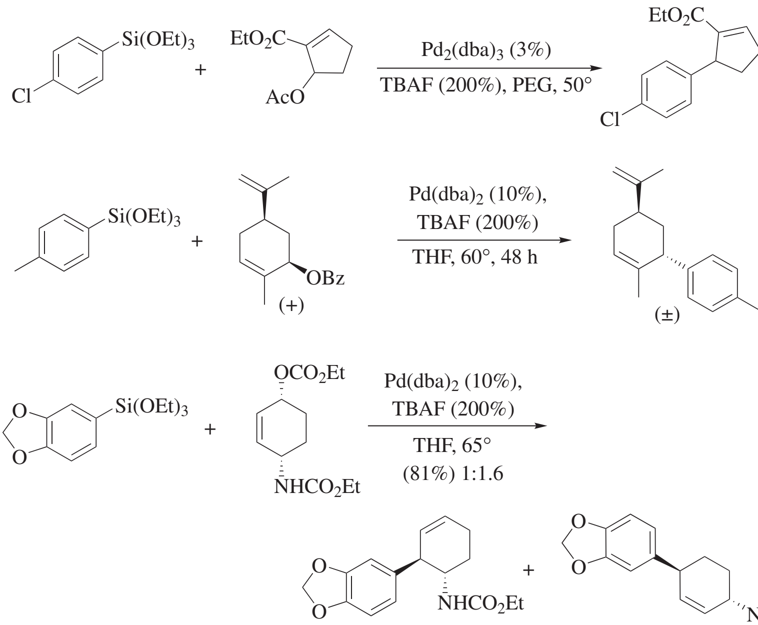


(Eq. 139)



(Eq. 140)

Cyclic Electrophiles. Arylation of cyclic allylic carboxylates with equivalent substitution at the allylic termini proceeds under standard conditions in modest to good yields and with high *anti* selectivity with respect to the starting carboxylate (Eqs. 141 and 142).[253,255] However, the site selectivity in unsymmetrically substituted electrophiles is poor (Eq. 143).[253]



(Eq. 141)

(Eq. 142)

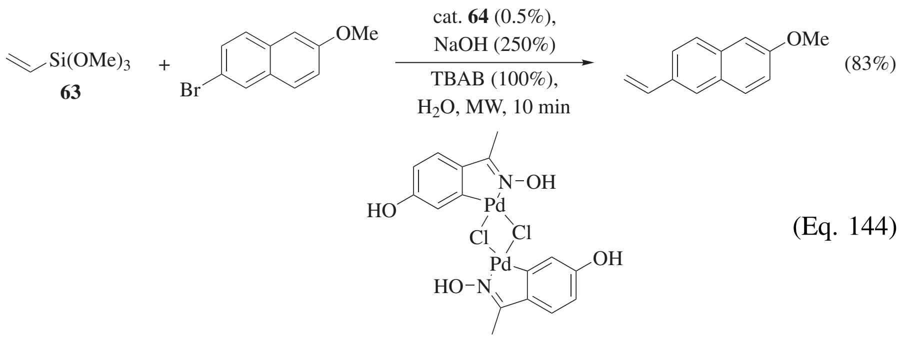
(Eq. 143)

Alkyl Halides. An important recent development in asymmetric substitution of aliphatic halides involves the combination of aryltrimethoxysilanes with racemic α-bromo esters in the presence of the chiral ligand (*S*,*S*)-**44** and a fluoride source (TBAT) to provide the α-aryl carboxylic esters in high yields and enantioselectivities (Eq. 25).[118] The bulky BHT ester is essential for high enantioselectivity.

Alkenyl-TGs

The vast majority of examples of this donor group employ the parent vinyltrimethoxysilane for simple vinylation[62,70,87] or as a linking group in the preparation of vinylenearylene polymers.[256]

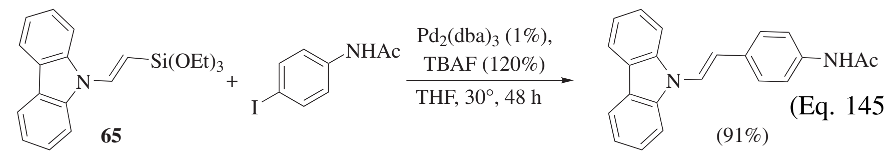
Aryl Halides. Direct vinylation of aromatic bromides and chlorides with vinyltrimethoxysilane (**63**) can be accomplished in aqueous NaOH with tetra-*n*-butylammonium bromide (TBAB) and either palladium acetate or palladacycle catalyst **64** under microwave heating (Eq. 144).[257] This method has also been employed for cross-coupling of (*E*)-styryltrimethoxysilane.



64

(Eq. 144)

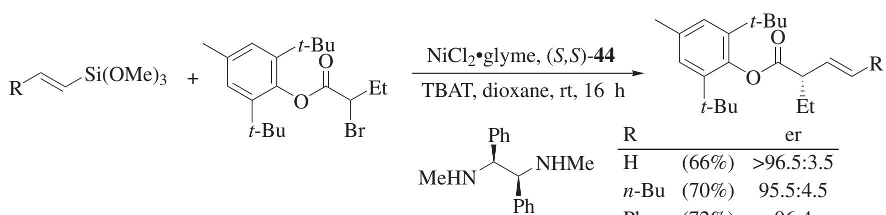
(*E*)-*N*-Styrylcarbazoles can also be prepared by cross-coupling of the silylalkenylcarbazole reagent **65**, which itself is prepared by a silylative coupling reaction of **63** with 9-vinylcarbazole. The cross-coupling reaction takes place under standard conditions with a variety of aryl iodides (Eq. 145).[258]



(Eq. 145)

Allylic Carboxylates. Vinylation of allylic carboxylates with **63** under fluoride activation affords 1,4-dienes in a stereoconvergent fashion.[254]

Alkyl Halides. The enantioselective coupling of racemic α-bromo esters in the presence of a chiral ligand, (*S*,*S*)-**44**, and a fluoride source (TBAT) can also be effected with alkenyltrimethoxysilanes in good yields and high selectivities (Eq. 146).[118]



(*S*,*S*)-**44**

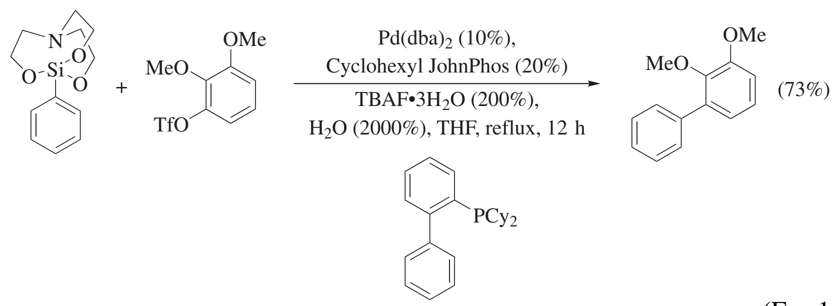
R		er
H	(66%)	>96.5:3.5
n-Bu	(70%)	95.5:4.5
Ph	(72%)	96:4

(Eq. 146)

Silatranes

Silatranes represent a unique class of trialkoxysilanes by virtue of the internal coordination of the silicon by the nitrogen atom.[259] These reagents have been

applied to the cross-coupling of aromatic triflates with moderate success.[260] As is the case with silanols, addition of water[202] is crucial to suppress the cleavage of the triflate in the presence of TBAF (Eq. 147). Oxidative addition is facilitated by the ligand Cyclohexyl JohnPhos (**66**).[200]



Cyclohexyl JohnPhos (**66**) (Eq. 147)

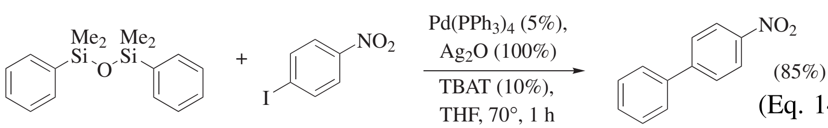
Cross-Coupling of Di- and Polysiloxanes

Disiloxanes are synthetic equivalents of silanols and polysiloxanes are synthetic equivalents of silanediols. In fact, the dimers and oligomers readily form from silanols and silanediols under acid or base catalysis. The oligomers can be engaged in cross-coupling under activation by either fluoride sources or by silanolate exchange with KOTMS.

Disiloxanes

Symmetrical Disiloxanes. Although only a limited number of symmetrical disiloxanes are commercially available,[201] they can be prepared by hydrosilylation of terminal alkynes with tetramethyldisiloxane[261] or by silylative coupling with divinyltetramethyldisiloxane (DVDS).[258]

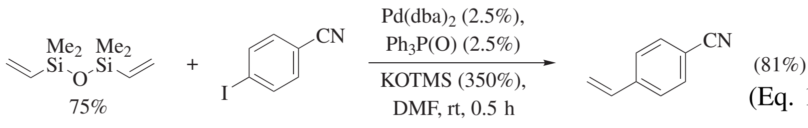
Aryl-TGs. A single report describes the cross-coupling of aryldimethyl disiloxanes with reactive aryl iodides and bromides under activation by silver oxide and TBAF or TBAT (Eq. 148).[201]



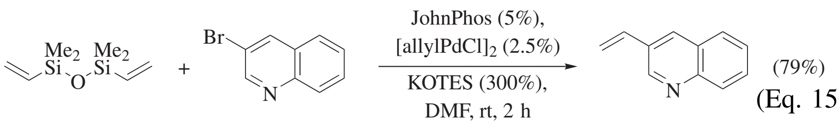
(Eq. 148)

Alkenyl-TGs. For the transfer of a simple vinyl group,[62] the commercially available and inexpensive reagent divinyltetramethyldisiloxane (DVDS) is ideal. Both vinyl groups are active and the atom economy of the reagent is high. The development of suitable conditions for vinylation with DVDS takes advantage of Design of Experiment protocols (DoE) to generate the reactive species potassium

vinyldimethylsilanolate in situ by a silanolate exchange reaction with KOTMS or potassium triethylsilanolate (KOTES).[262] A wide range of aromatic iodides (Eq. 149) and bromides (Eqs. 150 and 151) undergo vinylation in good yield under mild conditions. An *Organic Syntheses* procedure has been developed for the vinylation of bromides.[263]



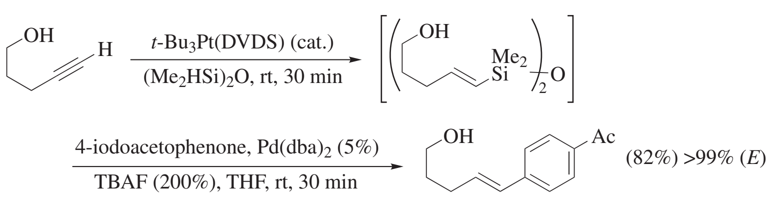
(Eq. 149)



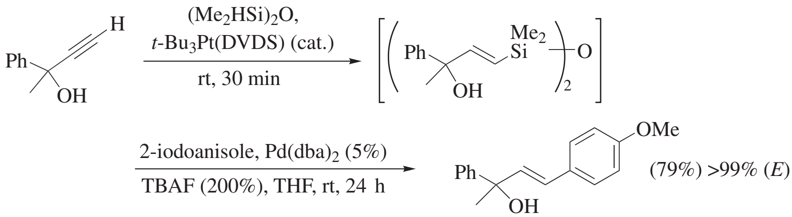
(Eq. 150)

(Eq. 151)

Symmetrical disiloxanes are also readily available from the highly site- and stereoselective hydrosilylation of terminal alkynes with tetramethyldisiloxane with Karstedt's catalyst.[197] The in situ generated disiloxanes undergo efficient cross-coupling under standard conditions ($Pd(dba)_2$/TBAF) to afford the (E)-styrenes with high selectivity; only traces of (Z)-isomers and internal isomers are detected (Eqs. 152 and 153).[261] Interestingly, cross-coupling with alkenyl iodides leads to a greater proportion of the internal isomer which must arise from a *cine* substitution.



(Eq. 152)

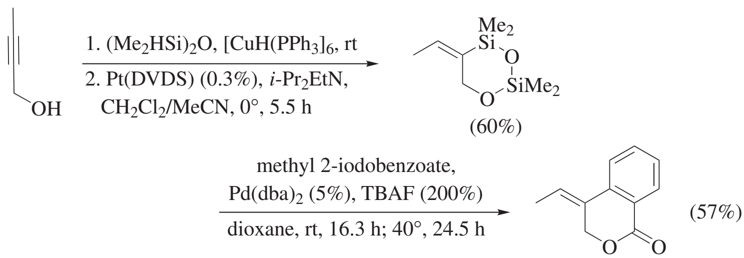


(Eq. 153)

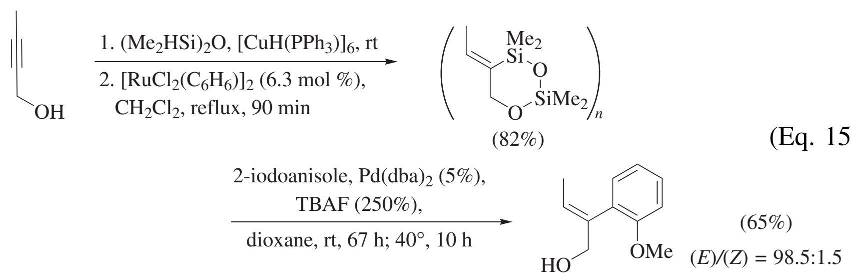
Unsymmetrical Disiloxanes. All unsymmetrical alkenyl disiloxanes used for cross-coupling are prepared by hydrosilylation of terminal alkynes with

unsymmetrical hydrosilanes. Hydrosilylation of terminal alkynes with pentamethyldisiloxane using $(Ph_3P)_3RuI$ as the catalyst affords both (E)- and (Z)-alkenylsilanes depending on the reaction conditions.[230] Cross-coupling under standard conditions with TBAF affords good yields of the styrenes or stilbenes, albeit with a narrow substrates scope.

The intramolecular version of this reaction employs either platinum or ruthenium catalysts to effect the *syn* or *anti* hydrosilylation of a tethered alkene, followed by cross-coupling under standard reaction conditions to afford (Z)- and (E)-allylic alcohols, respectively (Eqs. 154 and 155).[264]



(Eq. 154)

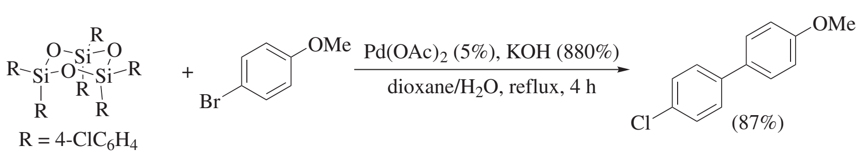


(Eq. 155)

Polysiloxanes

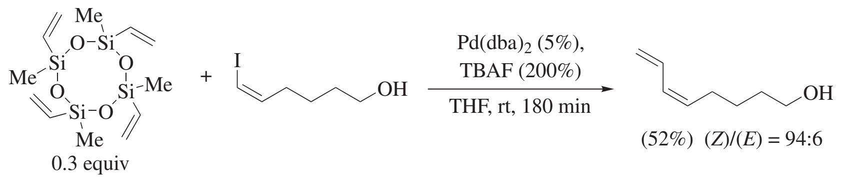
Trimers and Tetramers. A number of discrete oligomers of aryl and vinylsiloxanes are commercially available such as hexaphenylcyclotrisiloxane and tetramethyltetravinylcyclotetrasiloxane (D_4V). However, other aryl trisiloxanes can be prepared from aryldichlorosilanes by hydrolysis to the silanediol and acid-catalyzed dehydration.[265] In addition, silylative cross-coupling of D_4V with terminal alkenes affords higher homologs of the cyclic tetramers that are also competent in cross-coupling.[266]

Aryl-TGs. Three simple hexaarylcyclotrisiloxanes have been employed in cross-coupling reactions with aryl iodides, bromides, and chlorides under activation by KOH in the presence of $Pd(OAc)_2$ (Eq. 156). Under these conditions, all six aryl groups are transferred.

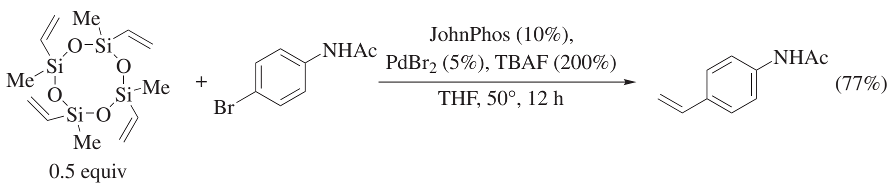


(Eq. 156)

Alkenyl-TGs. Simple vinylation of aromatic iodides and bromides is effected under mild conditions with fluoride activation using D_4V.[267] The reagent is the least expensive of the commercially available silicon-based vinylating reagents and all four vinyl groups are transferred (0.3 equiv of D_4V).[62] The cross-coupling of aryl and alkenyl iodides proceeds at room temperature without added ligands, whereas the coupling of aryl bromides requires 50° and a bulky phosphine ligand to facilitate oxidative addition (Eq. 157, 158). Moreover, the slower coupling of the aromatic bromides led to the formation of secondary products derived from a Heck coupling which can be suppressed by increasing the loading of D_4V to 0.5 equiv. An *Organic Syntheses*[263] procedure has been developed for the coupling of a heteroaryl bromide.



(Eq. 157)



(Eq. 158)

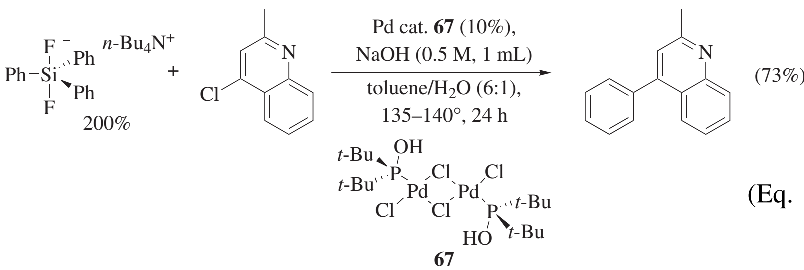
Oligomers. Two commercially available silicones have been used for the transfer of phenyl and alkenyl groups. Polyphenylmethylsilicone undergoes cross-coupling with aryl iodides under activation by silver(I) oxide and $(Ph_3P)_4Pd$. For the transfer of alkenyl groups, polymethylhydridosilane (PMHS) is employed in platinum-catalyzed hydrosilylation of terminal alkynes to prepare (*E*)-alkenylsilicones that transfer the alkenyl group to aryl iodides under activation by TBAF and $Pd_2(dba)_3 \cdot CHCl_3$.[268]

Cross-Coupling of Siliconate Complexes

The early recognition that for effective transmetalation from silicon to palladium the silicon moiety must be anionically activated led to the introduction of a number of stable siliconate complexes for cross-coupling. Stable siliconates bearing fluorine and oxygen atoms have been prepared and are competent in cross-coupling with aryl, heteroaryl, and allyl electrophiles. Siliconates are reactive anionic complexes that have limited substrate scope and are not atom economical. Accordingly, these reagents have, for the most part, been supplanted by more easily prepared, readily available, and less sensitive reagents.

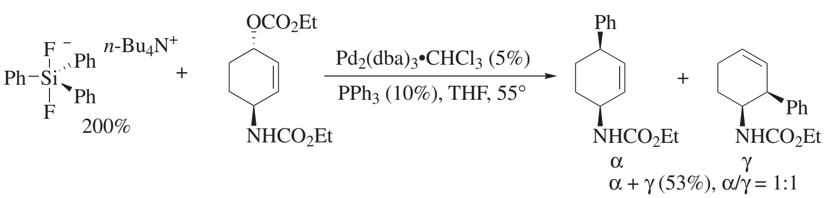
Fluorosiliconates

Difluorosiliconates. This category contains only one species, TBAT, which can transfer but a single phenyl group from the three attached to silicon.[69,269] This inefficiency is compounded by the need to use multiple equivalents of the reagent. Other combinations of phenyl and methyl groups on a difluorosilicate have been investigated, but these give poorer yields of coupling products than TBAT.[270] Phenylation with TBAT can be effected without additional activators in DMSO or DMF at elevated temperature or with aqueous NaOH (also at elevated temperature). Aromatic iodides, bromides, and triflates participate in the coupling and in some cases, activated chlorides as well. Heteroaromatic bromides and chlorides (pyridines, quinolines, and thiophenes) couple effectively in the presence of dimeric palladium(II) phosphinous acid complex **67**, which operates in hot (135°) aqueous NaOH (Eq. 159).



(Eq. 159)

Allylic benzoates and carbonates undergo phenylation with TBAT in a net invertive displacement process; however, the site selectivity is highly substrate dependent (Eq. 160).[111]



(Eq. 160)

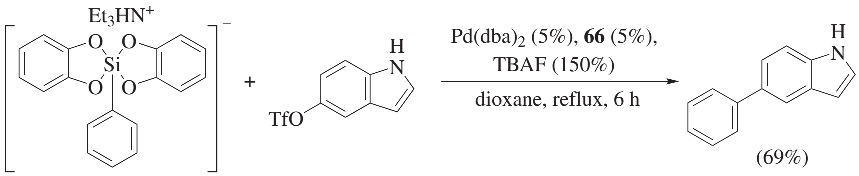
Pentafluorosiliconates. These hypercoordinate species (prepared by treatment of organotrichlorosilanes with KF)[271] were the first silicon reagents to demonstrate potential in palladium-catalyzed cross-coupling reactions.[21] Prior studies had shown the ability of pentafluorosiliconates to undergo oxidative dimerization[21,272,273] or carbonylation[274] reactions to form esters. The best described cross-coupling reaction of these salts is the reaction with allylic halides, but the halide is used in 10-fold excess.[21] Aside from providing a soluble, anhydrous source of fluoride, TASF can also deliver methyl groups to activated aromatic bromides and iodides.[275]

Catecholsiliconates

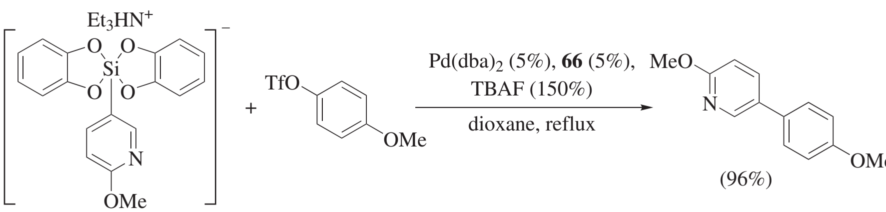
The synthesis, structure, and properties of pentacoordinate catecholsiliconates have been the subject of extensive studies.[17–20] However, their use as reagents

for carbon-carbon bond formation did not materialize until a 1988 report on the coupling of alkenylsiliconates with aryl iodides and triflates.[22,87] Most of these coupling reactions involve the parent vinylsiliconate because the more substituted alkenylsiliconates give a significant amount of the *cine* substitution products (Eq. 20).

Aromatic and heteraromatic siliconates are well suited for cross-coupling with aromatic and heteroaromatic triflates.[276] The siliconates are easily prepared from the aromatic trialkoxysilicates by treatment with catechol and triethylamine in alcoholic solution. The reaction conditions generally employ $Pd(dba)_2$, ligand **66** (Eq. 147), and TBAF in refluxing THF or dioxane. Good functional-group compatibility is seen for the electrophile, but the nucleophile is limited to the availability of the arylsiliconate (Eqs. 161, 162).



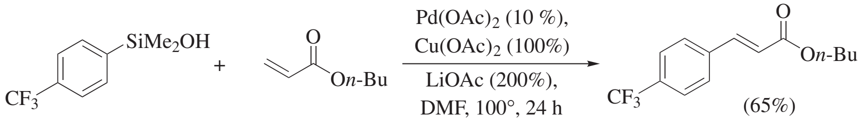
(Eq. 161)



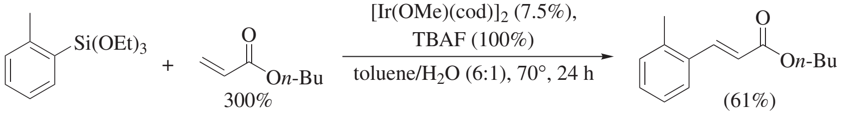
(Eq. 162)

Oxidative Heck Reactions

Although beyond the scope of this chapter, a number of silanols, silanediols, and siliconates undergo oxidative Heck-type reactions with activated alkenes under catalysis by palladium(II) acetate and a stoichiometric amount of copper(II) acetate[203,277,278] (Eq. 163) or with an iridium(I) catalyst and a sacrificial alkene as the oxidizing agent (Eq. 164).[279]



(Eq. 163)



(Eq. 164)

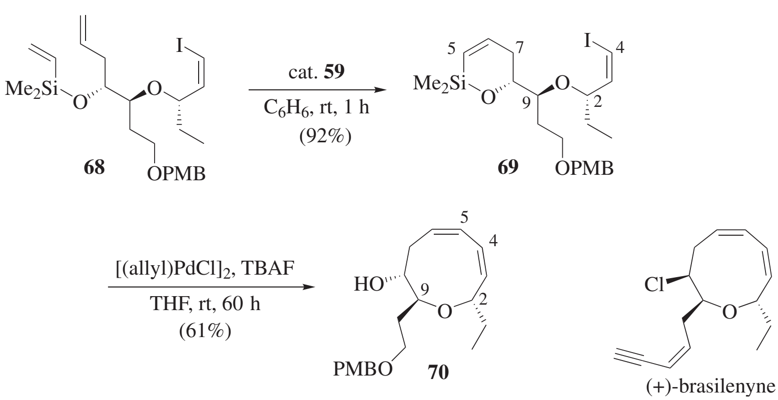
APPLICATIONS TO SYNTHESIS

Overview

The diversity of transferable groups and organo electrophiles that participate in cross-coupling reactions mediated by myriad silicon moieties is amply illustrated in the "Scope and Limitations" section. Silafunctional derivatives of alkynes, arenes, heteroarenes, alkenes, and to a limited extent alkanes can deliver the transferable group efficiently to halides and sulfonates derivatives of a similar set of organic residues. Accordingly, these methods have been featured in a number of total syntheses of natural products. The examples selected below highlight some of the unique features of silicon-based cross-coupling.

Total Synthesis of Natural Products

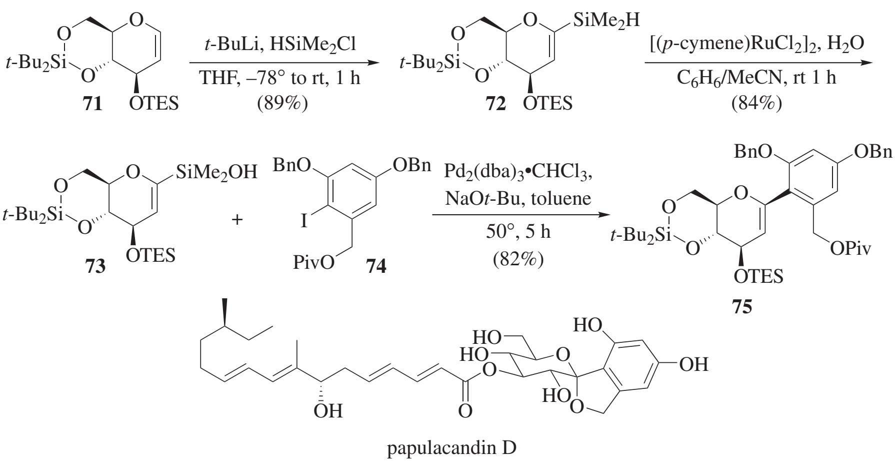
(+)-Brasilenyne.[228,229,280] (+)-Brasilenyne is a marine antifeedant isolated from the digestive gland of a sea hare (*Aplysia brasiliana*). The most prominent structural feature of brasilenyne is the nine-membered cyclic ether bearing a 1,3-*cis,cis*-diene unit. The key precursor **68**, which contains all of the carbons and the stereocenters needed for brasilenyne, is poised for a sequential ring-closing metathesis/cross-coupling reaction to install the key diene unit and construct the oxocene ring (Eq. 165). The amalgamation of the powerful ring-closing metathesis process (RCM) with a silicon-based cross-coupling reaction allows for a general synthesis of medium-sized rings containing a 1,3-*cis,cis*-diene unit (cf. Scheme 20). Silyl ether **68** is first subjected to a highly efficient RCM reaction using Schrock's catalyst (**59**; Scheme 19) to afford six-membered cyclic alkenylsilyl ether **69**. In the subsequent cross-coupling reaction, the six-membered siloxane ring is transformed by the combination of TBAF and $[(\pi\text{-allyl})PdCl]_2$ to the nine-membered ring ether **70** through the formation of the C(4)−C(5) bond. The stereospecificity of the cross-coupling process assures the specific generation of the (Z,Z)-conjugated diene at the desired position in the nine-membered ether. The synthesis of (+)-brasilyene could then be completed by a straightforward introduction of chlorine at C(8) and elaboration of the enyne side chain following a literature precedent.



(Eq. 165)

(+)-Papulacandin D.[214,215] The papulacandins are a family of antifungal agents, isolated from the deuteromycetous fungus *Papularia sphaerosperma*, that have demonstrated potent in vitro antifungal activity against various pathogens. All of the papulacandins are amphipathic molecules composed of an aromatic moiety linked via a spirocyclic structure to a lactose moiety with two different aliphatic acyl side-chains. The simplest member of the family, papulacandin D, lacks the *O*-(6′-acyl-β-galactoside) at the O(4) position. The key strategic disconnection for the synthesis of papulacandin D requires the cross-coupling of a 2-pyranylsilanol with an aryl halide (Scheme 21). Although α-oxyalkenylsilanols are competent substrates for cross-coupling, the requirement for fluoride activation is clearly incompatible with the silyl ether protecting groups planned in the total synthesis. Therefore, fluoride-free conditions for the cross-coupling had to be developed.

The actual synthesis requires the cross-coupling of the glycal silanol **73** with the protected iodo resorcinol derivative **74** (Scheme 21). To prepare **73**, silyl-protected glycal **71** is lithiated at C(1) followed by capture with chlorodimethylsilane. The resulting hydrosilane **72** is subjected to a ruthenium-catalyzed, oxidative hydrolysis to afford the base-sensitive silanol **73**. The key cross-coupling reaction is quite challenging because of protiodesilylation of **73**, but ultimately this critical transformation could be achieved efficiently using sodium *tert*-butoxide as the Brønsted-base activator and $Pd_2(dba)_3$•$CHCl_3$ as the catalyst to provide *C*-arylglycal **75** in good yield. Glycal **75** contains the entire carbon framework of the sugar fragment of papulacandin D.

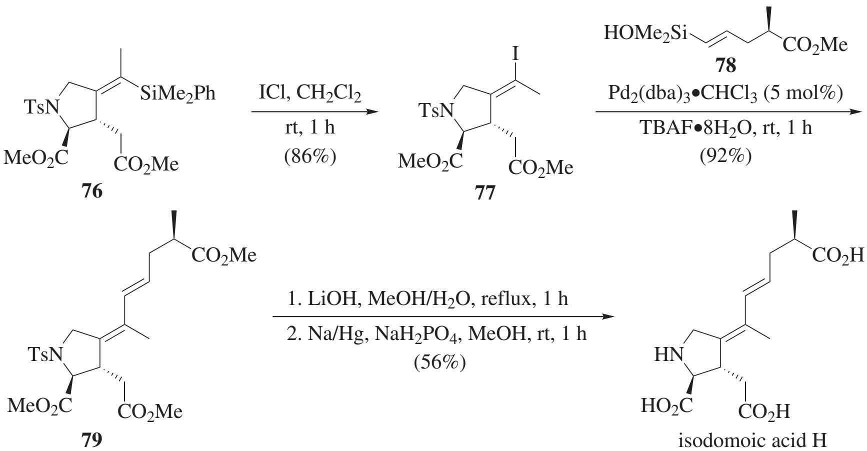


papulacandin D

Scheme 21

(+)-Isodomoic Acids G and H.[281,282] Whereas the two target molecules described above are oxygenated natural products, the neuroactive marine natural products, isodomoic acids G and H, were the first alkaloids synthesized via silicon-based cross-coupling. The initial strategic connection of these targets was inspired by the sequential silylcarbocyclization/cross-coupling reactions

(Eq. 45) involving a silicon-based donor related to **76** and a 5-iodopentenoate acceptor related to **78**. Surprisingly, after an extensive survey of conditions, none of the key cross-coupling product **79** could be detected. The failure to effect this coupling led to a reversal in the roles of the donor and the acceptor (Scheme 22).

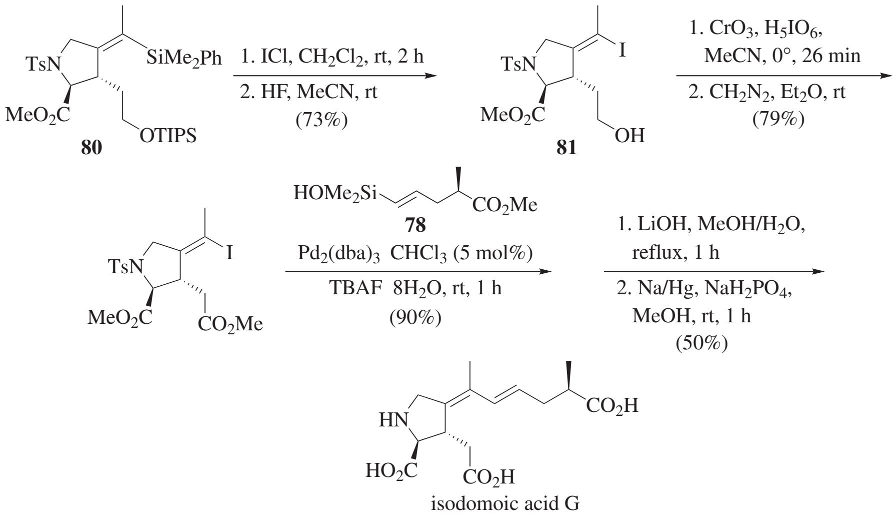


Scheme 22

Accordingly, treatment of alkenylphenyldimethylsilane **76** with iodine monochloride effects an iododesilylation that proceeds with a complete *inversion* of double bond configuration, presumably through an anchimeric participation of the neighboring carbonyl group. In the key cross-coupling reaction of **77**, the fluoride hydration level plays a critical role. When the TBAF is tri-, tetra- or hexahydrated, the conversion is modest and the reaction stalls within 2 h. However, the reaction rate improves dramatically by employing TBAF•$8H_2O$. With this activator, the coupling with silanol **78** proceeds rapidly to afford the protected isodomoic acid H, **79**, in 92% yield. The synthesis is completed by the saponification of the three methyl esters of **79** using LiOH, followed by a detosylation using sodium amalgam to afford isodomoic acid H.

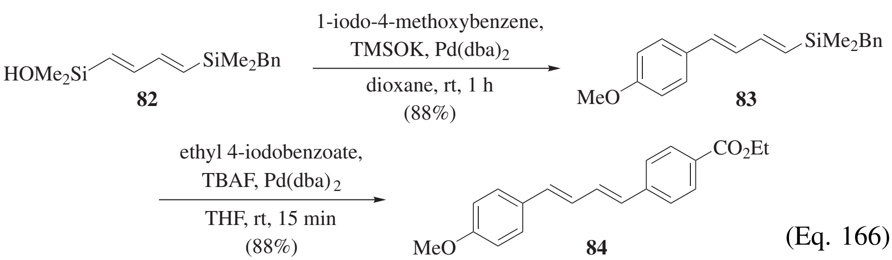
The invertive iododesilylation pathway could be suppressed by employing **80** in which the triisopropylsilyl ether prevents the anchimeric participation of the ether oxygen, thus enabling the synthesis of isodomoic acid G (Scheme 23). Treatment of **80** with iodine monochloride proceeds with exclusive *retention* of double bond configuration, affording (E)-alkenyl iodide **81** in 73% yield. (E)-Alkenyl iodide **81** is subjected to the same sequence of cross-coupling with **78** and deprotection as described above, to achieve the total synthesis isodomoic acid G.

(+)-RK-397.[216,283] The silicon-based cross-coupling reaction is mechanistically unique in that two different modes of transmetalation are possible. This mechanistic duality has significant preparative utility because the different mechanistic pathways can be accessed via complementary reaction conditions. The feasibility of using both modes of activation in a single reagent is illustrated by



Scheme 23

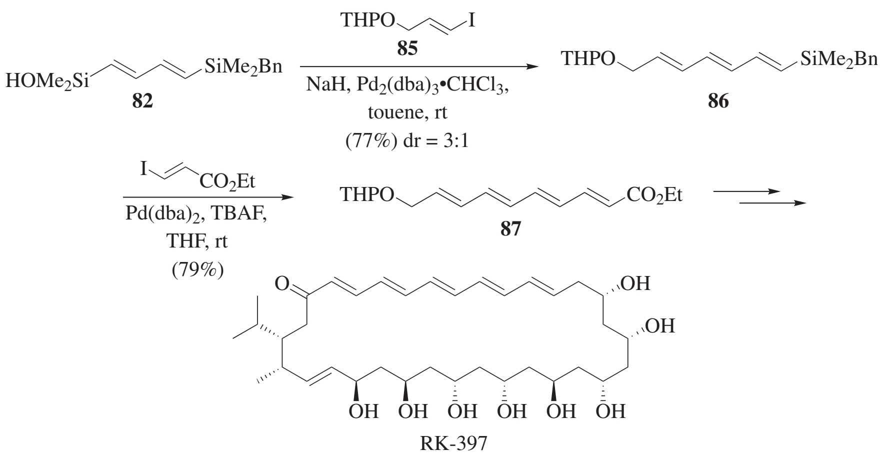
sequential Brønsted base/fluoride-promoted cross-coupling reactions using the linchpin reagent (E,E)-[(4-benzyldimethylsilyl)-1,3-butadienyl]dimethylsilanol (**82**). This bifunctional reagent can combine with two electrophiles under complementary conditions for the construction of unsymmetrical polyenes. In the first cross-coupling reaction, **82** is treated with KOTMS in the presence of an aryl iodide and $Pd(dba)_2$ to afford the (1-aryl-1,3-butadienyl)benzylsilane **83**. The benzyldimethylsilyl group is inert under these conditions. Subsequently, treatment of **83** with TBAF effects the second cross-coupling reaction which proceeds smoothly to afford the unsymmetrical 1,4-diaryl-1,3-butadiene **84** (Eq. 166).



(Eq. 166)

The total synthesis of the polyene-polyol antifungal agent RK-397 aptly demonstrates the power of complementary modes of activation for silicon-based cross-coupling reaction (Scheme 24). Whereas in the above synthetic study both electrophiles are *aryl* iodides, the construction of the polyene fragment of RK-397 requires the cross-coupling reaction with two *alkenyl* iodides. This extension is challenging because alkenyl iodides are less reactive. Thus, for the cross-coupling

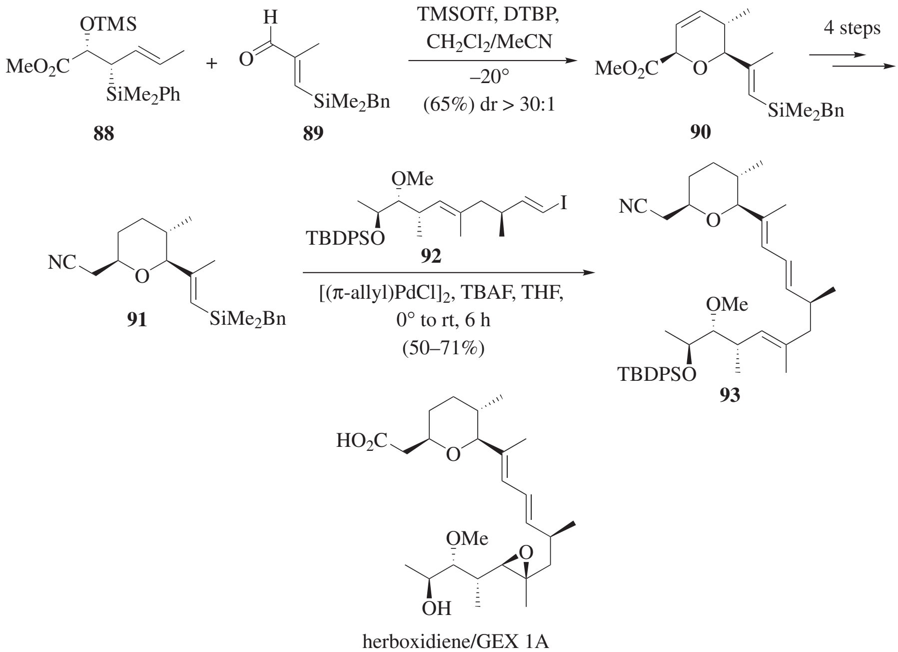
of **82** with alkenyl iodide **85**, NaH is employed instead of KOTMS as the Brønsted base promoter. The stoichiometric generation of the silanolate using a strong base such as NaH provides heightened reactivity. The resulting triene **86** is then combined with ethyl (*E*)-3-iodopropenoate under fluoride-promoted cross-coupling conditions to afford tetraene **87**. This key fragment is then incorporated into the polyol fragment, completing the total synthesis of RK-397.



Scheme 24

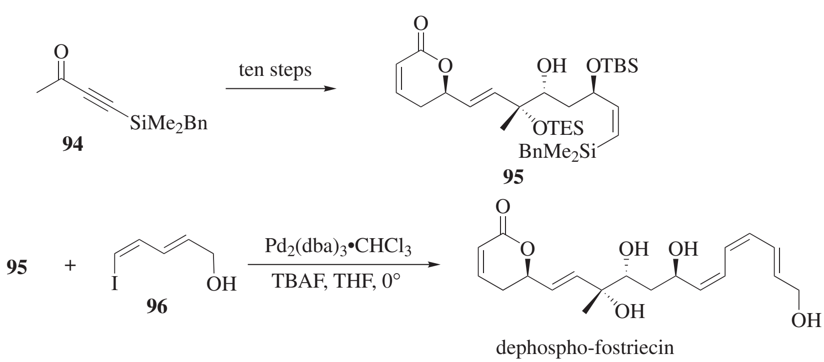
Herboxidiene/GEX IA.[284] An important feature of silicon-based cross-coupling reactions for complex molecule synthesis is the stability of organosilicon groups to many different reaction conditions. Because of this feature, the silicon can be introduced early in the synthetic route (if the strategy calls for it) and can be carried through until the key bond-forming process is called into service. The total synthesis of the phytotoxic antitumor compound herboxidiene/GEX 1A highlights this empowering feature of silicon-based cross-coupling reactions (Scheme 25). In the early stage of the synthesis, allylsilane **88** and (*E*)-3-benzyldimethylsilylmethacrolein (**89**) are combined in a Lewis acid promoted [4 + 2] annulation reaction to prepare **90**, a dihydropyran bearing an alkenylbenzyldimethylsilyl group. This "masked" equivalent of an alkenylsilanol is carried through four steps that involve an aggressive reducing agent (lithium aluminum hydride), a basic nucleophile (4-dimethylaminopyridine), and elevated temperature (refluxing DMF), to arrive at the cross-coupling substrate **91**. Treatment of benzylsilane **91** with TBAF and [allylPdCl]$_2$ promotes the cross-coupling with a fourteen carbon fragment, alkenyl iodide **92**, to afford the advanced intermediate **93**, which possesses the complete carbon skeleton of herboxidiene/GEX 1A.

Dephospho-Fostriecin. An extreme example of the robustness of the benzyldimethylsilyl group to be carried through many synthetic transformations is illustrated in the formal synthesis of fostriecin, a cytotoxic phosphate ester isolated from *Streptomyces pulveraceus* (Scheme 26). The silyl moiety is introduced



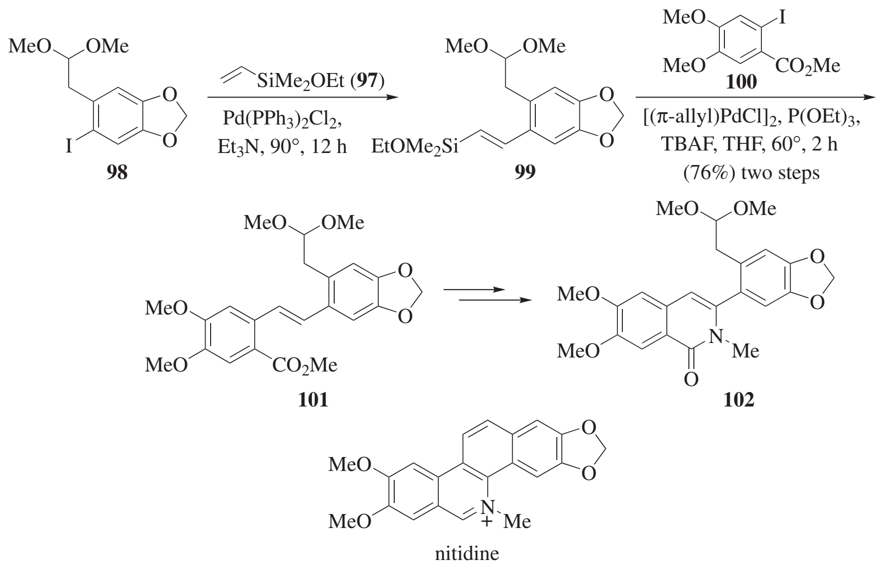
Scheme 25

very early in the synthetic route (structure **94**) and survives the next ten steps, which include aldol addition, hydrogenation, acidic hydrolysis, organomagnesiate coupling, acylation, ring-closing metathesis, and diimide reduction, to reach intermediate **95**. A fluoride-mediated cross-coupling of **95** with **96** (with concomitant deprotection) completes the synthesis of dephospho-fostriecin **97**.



Scheme 26

Nitidine.[285] The formal total synthesis of the anti-leukemic compound nitidine employs an interesting Heck/cross-coupling reaction sequence to unite the two oxygenated benzene subunits in stilbene **101** (Scheme 27). The commercially available building block ethoxydimethylvinylsilane (**97**) serves as a linchpin reagent through an interesting Heck reaction/cross-coupling sequence, to assemble the carbon skeleton of the target molecule **102**, thus intercepting a previous synthesis of nitidine.[286] In the first step of this sequential process, aryl iodide **98** undergoes a Heck reaction with ethoxydimethylvinylsilane catalyzed by $Pd(PPh_3)_2Cl_2$ to afford ethoxydimethylstyrylsilane **99**. Without purification, **99** is combined with aryl iodide **100**, and the mixture is treated with TBAF in the presence of $[allylPdCl]_2$ to afford the cross-coupling product **101** in 76% yield.



Scheme 27

COMPARISON WITH OTHER METHODS

In the year after the Nobel Prize for cross-coupling reactions (2010), the challenge of comparing the utility and impact of silicon-based cross-coupling methods to the venerable Suzuki, Stille, and Negishi reactions is daunting. Furthermore, recent analyses of reactions commonly used in the discovery and process departments of pharmaceutical companies show a high and increasing percentage of carbon-carbon bond construction through the classical cross-coupling processes.[287] This trend is self-fulfilling as more and more sophisticated building blocks containing boronic acids or their surrogates become commercially available.

Direct comparisons among the various methods are rare and further complicated by the dozens of different organosilicon donors that are able to accomplish a given transformation. Accordingly, only generalizations will be provided here.

In terms of reaction scope, there are no major classes of cross-coupling with organosilicon donors that cannot also be done with boron, tin, or zinc. Indeed, the opposite is true for aliphatic transferable groups that can be coupled via stannanes[15] or trifluoroborates,[288,289] but not with silicon donors. In addition, carbonylative processes and reactions with acid chlorides are better effected with stannanes.[13,14] However, an important corollary to this statement is that the comparable performance of the silicon-based processes to the tin-based processes lends a distinct advantage to silicon in view of the lower cost, lower molecular weight, and significantly lower toxicity of the starting materials, intermediates, and waste products.

These issues notwithstanding, the silicon-based cross-coupling reactions do offer important advantages for a number of significant applications: (1) vinylation to form styrenes, (2) hydrolytically or stereochemically labile boron derivatives, (3) chemical robustness in multistep synthesis, and (4) constructive introduction of silicon. First, a cost and atom-efficiency analysis of commercially available vinylating reagents shows that vinylsilicon reagents are significantly more cost-effective than either boron- or tin-based vinylating reagents.[62] Second, the requirement for protic media in most Suzuki cross-coupling reactions often leads to undesired protiodeboronation of the precursor. This problem can be addressed by the use of anhydrous silanolate salts as is illustrated in the cases of sodium *N*-Boc 2-indolylsilanolates[208] and 2,6-dichlorophenyldimethylsilanolate.[54] In addition, the cross-coupling of alkenylboronic acids can be attended by loss in stereospecificity,[210,290] again a problem obviated by the use of alkenylsilanolate salts.[80] Third, the stability of organosilicon donor moieties is amply illustrated in many total synthesis endeavors whereby conditions not likely to be tolerated by boronic acids are successfully employed. However, this advantage is now being challenged by the introduction of robust protecting groups for boronic acids.[291,292] Finally, the myriad transformations for introduction of organosilicon donor groups that can then be combined with cross-coupling in a telescoped sequence (as illustrated in the total syntheses of brasilenyne and isodomoic acids G and H) offer unique advantages to the silicon-based cross-coupling approach.[158]

EXPERIMENTAL CONDITIONS

Preparation of Organosilane Precursors

The evolution of silicon chemistry in organic synthesis over the past 40 years has yielded a wealth of preparatively useful methods for the introduction of organosilicon moieties into organic compounds.[4] In addition, and partly thanks to the silicone polymer industry, a large number of inexpensive silicon-containing building blocks are commercially available. Among the most common are: $SiCl_4$, $HSiCl_3$, Me_2SiHCl, Me_2SiCl_2, $(ClMe_2Si)_2$, $(Me_2HSi)_2O$, $(MeO)_3SiCl$, and $(Me_2\text{-}SiO)_3$ (D_3). In addition, an increasing number of reagents are becoming

available for direct cross-coupling including D_4V, DVDS, vinylMe_2SiCl, allylMe_2SiCl, $PhSi(OMe)_3$, $(Ph_2SiO)_3$, etc.

The construction of carbon-silicon bonds in organic substrates can be accomplished by four basic strategies: (1) addition of organometallic nucleophiles to silicon electrophiles, (2) hydrosilylation and its manifold variants, (3) silylative coupling and metathesis, and (4) insertion wtih silanes or disilanes. Each of these strategies is described in detail below.

Additions to Silicon Electrophiles. Organolithium and -magnesium reagents derived from all classes of transferable groups react readily with chlorosilanes but these transformations can be complicated by multiple additions to polyhalosilane precursors. Solutions to this problem include the use of a large excess of the inexpensive halosilane or the use of masking groups such as dialkylamino groups that can later be converted into chloro groups by treatment with PCl_3 or $AsCl_3$. Alternatively, hydridochlorosilanes offer the advantage of containing but a single nucleofuge, leaving behind a silicon hydrogen bond that can be easily converted into a halogen (Cl_2 or SO_2Cl_2) or oxygen ($H_2O/[(C_6H_6)RuCl_2]$). Organolithium reagents are considerably more reactive than organomagnesium reagents for this purpose and the reactivity of the silicon electrophile decreases with decreasing numbers of chlorides and increasing size of the organic residues. The resulting chlorosilanes can be readily converted to fluorosilanes by treatment with copper(II) fluoride,[173] antimony(III) fluoride, or fluorosilicates.[188] Hexamethylcyclotrisiloxane (D_3) is one of the most useful reagents for the introduction of a dimethylsilanol unit, but it reacts only with organolithium reagents (Eq. 75).

Hydrosilylation. Hydrosilylation of alkynes is a well-established, workhorse method for introducing organosilyl functional groups with controllable site and stereoselectivity.[223] Many hydrosilanes bearing chloro, alkoxy, silyloxy, and alkyl substituents are commercially available. For the hydrosilylation of terminal alkynes, transition-metal catalysts can selectively control the site of carbon-silicon bond formation. Thus, platinum catalysts (e.g., H_2PtCl_6, (DVDS)Pt-(t-Bu_3P))[197] react via a *syn* hydrosilylation process to afford (E)-1-alkenylsilanes, whereas $[(aryl)RuCl_2]_2$ promotes an *anti* hydrosilylation process to afford (Z)-alkenylsilanes,[198] and the cationic ruthenium complex $[(Cp)Ru(MeCN)_3]^+ PF_6^-$ reverses the site selectivity to afford 2-alkenylsilanes.[159]

Hydrosilylation of alkynes (and its carbonylative cousin) can also be carried out intramolecularly to set alkene geometry for subsequent cross-coupling processes. Moreover, the various incarnations of silylcarbocyclization allow for the construction of rings as part of the hydrosilylation process.[293,294]

Silylative Coupling and Metathesis. The construction of alkenylsilanes by silylative coupling superficially resembles cross-metathesis, but in fact is a mechanistically distinct dimerization with loss of ethylene to form higher alkenylsilanes or 1,2-disilylethenes.[219–221] A variety of ruthenium catalysts are effective

for this transformation, the most common of which is $RuHCl(CO)(PCy_3)_2/CuCl$. Moreover, the process can employ a wide range of vinylsilane precursors bearing alkyl, aryl, and alkoxy groups on silicon and alkenyl coupling partners bearing aryl, alkyl, alkoxy, and amino groups on the double bond. Finally, oligomeric vinylsiloxanes can be homologated to higher alkenylsiloxanes by this method.

Cross-metathesis and ring-closing metathesis of allylic silanes[295] and silyl ethers[296] is an established method for introducing allylic silane moieties.[297]

Insertion with Hydrosilanes and Disilanes. Transition-metal-catalyzed insertion of aryl iodides and bromides into silicon-hydrogen bonds provides a mild method for the formation of arylsilanes that would not be compatible with organometallic addition to silicon electrophiles. However, this transformation is complicated by the reduction of the halide in different types of aromatic substrates.[168,298–300] An alternative method that obviates the problem of reduction is the insertion with a disilane. This process allows the introduction of simple trialkylsilanes[199,301] as well as alkoxysilanes[199] by appropriate choice of disilane precursor.

Experimental Variables

As with all cross-coupling reactions, many experimental variables are critical to the success of the organosilicon-based process. However, this family of coupling reactions is further complicated by the large number of different organosilicon precursors and the different modes of activation of the silanes to effect the coupling process. Given the large number of possible permutations, selecting the "best conditions" for a new transformation is a formidable challenge. [In passing, the advantages of using a Design of Experiment optimization approach cannot be overemphasized.][262] The following sections provide general guidelines for the initial selection of components for all silicon-based cross-coupling reactions along with specific recommendations for special classes.

Palladium Source.[302] All of the common palladium sources employed for Stille and Suzuki cross-coupling reactions are also used for silicon-based cross-coupling. Nickel(II) sources have been used only with aliphatic halides and although highly useful, only NiX_2•diglyme has been employed.

Palladium(0). Although these sources obviate the need for in situ reduction to form an active catalytic species, they have varying degrees of oxygen sensitivity ranging from robust ($Pd(dba)_2$, $Pd_2(dba)_3$•$CHCl_3$ and their congeners) to highly air sensitive ((t-$Bu_3P)_2Pd$) and some of the more common in between (e.g., $(Ph_3P)_4Pd$). This category also contains in situ generated palladium nanoparticles. Such "ligandless" palladium catalysts have high activity, but can be plagued with low turnover number (TON) through precipitation of palladium black.

Palladium(II). These catalyst sources have the advantage of being air stable and generally less expensive than Pd(0) sources. They are available in two varieties, inorganic salts ($PdCl_2$, $Pd(OAc)_2$, $(NH_3)_2PdCl_2$) and ligated complexes ($(Ph_3P)_2PdCl_2$, $(PhCN)_2PdCl_2$, (dppf)$PdCl_2$, [allylPdCl]$_2$, (t-$Bu_2POH)PdCl_2$).[303]

The ligated complexes allow the precise stoichiometry of the ligand to be controlled. Alternatively, the use of $[allylPdCl]_2$ allows many different ligands to be introduced because the reduction of this precatalyst affords "ligandless" palladium(0).[304]

Palladium(I). This novel class of palladacycle, exemplified by compound **55** (Eq. 87),[212] has found application in challenging cross-coupling processes with aromatic bromides and chlorides.

Ligands. Over the past decade, the development of new ligands for palladium-catalyzed transformations has revolutionized the field by extending the scope of substrates that can be effectively coupled while simultaneously lowering catalyst loading and reaction temperatures.[305–309] Unfortunately, many of the early investigations on silicon-based cross-coupling did not benefit from these advances; only the more recent developments in the cross-coupling of trialkoxysilanes, silanols, and silanolates, and hydroxymethylphenyldimethylsilanes have incorporated the newer technologies. For the most part, the ligand choice is dictated by the electrophile and less so by the organosilicon donor. Nearly all of the ligands employed are phosphines; the advances in *N*-heterocyclic carbene ligands have not yet found their way into these coupling processes. However, olefinic ligands such as the dibenzylideneacetone family have proved useful in certain circumstances.[310]

Iodides. These most reactive substrates (as well as activated bromides) can couple without added ligands, although some form of stabilization of the Pd(0) species is often needed to prevent catalyst decomposition.

Bromides, Chlorides, and Sulfonates. To facilitate oxidative addition of the organohalide to the Pd(0) species, phosphine ligands of varying electronic properties and steric bulk are needed. In many cases, a trade-off between reaction temperature and donicity of the ligand allows for weaker ligands to be employed if higher temperatures can be tolerated. Among the weaker ligands are the arylphosphines such as Ph_3P, $(2\text{-tolyl})_3P$, $(2\text{-furyl})_3P$, dppp, dppb, and dppf. The bulkier, more electron-rich phosphines such as Cy_3P and $t\text{-}Bu_3P$ have enabled the cross-coupling of unreactive halides, as have the large class of biarylphosphane ligands (JohnPhos, SPhos, XPhos, RuPhos).[306,309]

Solvents. Many different solvents have found use in silicon-based cross-coupling reactions ranging from aromatic hydrocarbons (benzene, toluene) to ethereal solvents (THF, dioxane, DME) to dipolar aprotic solvents (DMF, DMSO, DMI) to water. For the majority of examples, THF and DMF are the solvents of choice, but at higher temperatures, these solvents (and especially dioxane) can often contribute to reduction of the organohalide. Water is a special case for the reaction of hydrolytically compatible organosilicon donors, trialkoxysilanes for the most part, in the presence of alkaline activators.

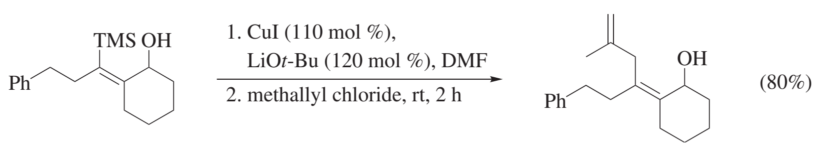
Additives. Aside from ligands for the palladium catalyst, occasionally other additives have been used to solve specific problems. For example, copper salts

have been used to suppress protiodesilylation or to facilitate slow transmetalation of the organosilicon donor to the palladium(II) intermediate.[81,208,213] Other additives have been employed to extend catalyst lifetime by stabilizing the Pd(0) nanoparticles with surfactants[234,254] such as tetra-*n*-butylammonium salts, sodium dodecylsulfate, or triphenylphosphine oxide.[218]

Fluoride Sources. A large majority of the known silicon-based cross-coupling reactions require a fluoride source to activate the silicon moiety to transmetalation. The most commonly employed sources are soluble tetralkylammonium fluorides such as TBAF•3H_2O, TMAF•4H_2O, and TEAF•2H_2O (TMAF = tetramethylammonium fluoride; TEAF = tetraethylammonium fluoride). The activity of the fluoride source is dependent on both the size of the ammonium cation as well as the hydration level. In a number of cases, Brønsted base promoted side reactions can be suppressed by increasing the hydration level with additional equivalents of water.[54,202,281,282,311] Anhydrous sources of fluoride have also been used, including KF, CsF, and the organic soluble siliconates TBAT and TASF. Although TMAF can be made anhydrous, it is only sparingly soluble, even in DMF.[312]

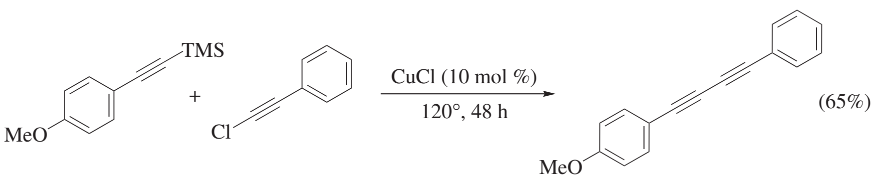
Brønsted Bases. The advent of organosilanols as viable donors in silicon-based cross-coupling, together with the discovery of a new mechanistic pathway involving the conjugate base silanolate salts, stimulated the introduction of a new class of activators. Initially, silver oxide[37] and silver carbonate were used, but these expensive agents can be replaced by the inexpensive and soluble alkali trimethylsilanolates.[32] Moreover, the discovery that the silanolates are self-activating allowed for the stoichiometric generation of the silanolate salts either in situ with strong bases such as sodium or potassium *tert*-butoxide, sodium or potassium hydride, or (in special cases) sodium hexamethyldisilazide.[55,208] Finally, many of the silanolate salts are stable, easily handled powders, and methods for the preparation and direct use of these reagents without added activators have been described.[54,80,108,209]

EXPERIMENTAL PROCEDURES

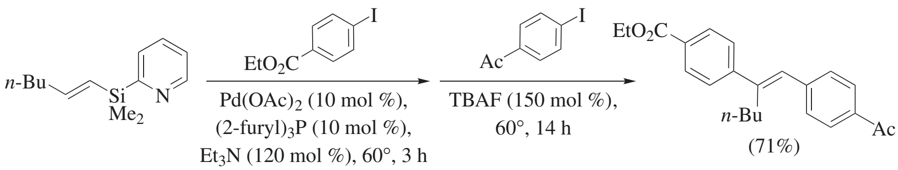


(Z)-2-(2-Methyl-6-phenylhex-1-en-4-ylidene)cyclohexanol [Hydroxyl-Assisted Allylation of an Alkenylsilane].[127] Copper(I) iodide (63 mg, 0.33 mmol) and DMF (1 mL) were placed in a flask and cooled to 0°. Lithium *tert*-butoxide (1 M in THF, 0.36 mL, 0.36 mmol) was added under argon and the

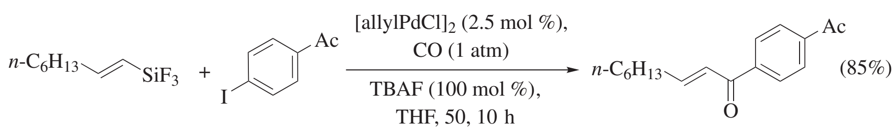
mixture was stirred for 20 min at rt. A DMF (1 mL) solution of (*Z*)-2-[3-phenyl-1-(trimethylsilyl)propan-1-ylidene]cyclohexanol (86 mg, 0.30 mmol) and a DMF (1 mL) solution of methallyl chloride (33 mg, 0.36 mmol) were successively added to the mixture. After the mixture was stirred for 2 h at rt, the reaction was quenched by addition of 3.5% aqueous NH_4OH solution. The organic materials were extracted with Et_2O, dried over Na_2SO_4, and concentrated. The residue was dissolved in THF (3 mL), and TBAF (1 M in THF, 0.3 mL, 0.3 mmol) was added to the solution. The mixture was stirred for 2 h at rt and diluted with water (15 mL). The organic materials were extracted with EtOAc, washed with 1 M HCl and water, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by PTLC (hexane/EtOAc, 4:1) to afford the coupling product (65 mg, 80%): IR (neat) 3369, 3064, 3026, 2931, 2854, 1645, 1603, 1496, 1452, 1373, 1350, 1335, 1255, 1227, 1176, 1142, 1093, 1074, 1045, 1030, 987, 964, 889, 748, 698 cm^{-1};^{1}H NMR δ 1.09–1.20 (m, 1H), 1.32 (bs, 1H), 1.40–1.53 (m, 2H), 1.71 (s, 3H), 1.70–1.82 (m, 2H), 1.89–1.95 (m, 1H), 2.11 (dt, J = 13.7 Hz, J = 3.4 Hz, 1H), 2.25–2.37 (m, 2H), 2.45 (d, J = 13.7 Hz, 1H), 2.63 (t, J = 8.2 Hz, 2H), 2.75 (d, J = 15.9 Hz, 1H), 2.87 (d, J = 15.9 Hz, 1H), 4.68 (s, 2H), 4.77 (s, 1H), 7.16–7.20 (m, 3H), 7.24–7.28 (m, 2H); ^{13}C NMR δ 20.1, 22.9, 25.1, 27.4, 33.7, 34.4, 35.2, 39.8, 66.7, 110.8, 125.8, 128.2, 128.3, 130.0, 136.8, 142.1, 144.4. Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.16; H, 10.15.



1-(4-Methoxyphenyl)-4-phenyl-1,3-butadiyne [Cross-Coupling of an Alkynylsilane with an Alkynyl Chloride].[133] To a solution of CuCl (2.4 mg, 0.02 mmol, 10 mol %) in DMF (1.5 mL) were added 1-chloro-2-phenylethyne (50 mg, 0.37 mmol) and [(4-methoxyphenyl)ethynyl]trimethylsilane (50 μL, 0.24 mmol) at rt. The reaction mixture was stirred for 48 h at 120°, quenched with 3 M HCl, and extracted with Et_2O (2 × 25 mL). The combined ethereal layers were washed with aqueous $NaHCO_3$ solution and brine and dried over $MgSO_4$. Filtration and evaporation provided a brown, oily residue. Column chromatography (silica gel, hexane/CH_2Cl_2, 10:1) afforded the diyne (36 mg, 65%) as a colorless solid: mp 96–97°; IR (KBr) 3076, 3056, 3035, 2216, 1599, 1506, 828 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.83 (s, 3H), 6.86 (d, J = 9.0 Hz, 2H), 7.30–7.58 (m, 7H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 55.3, 72.7, 74.2, 81.0, 81.8, 113.7, 114.2, 122.0, 128.4, 129.0, 132.4, 134.1, 160.4; HRMS (m/z): $[M]^+$ calcd for $C_{17}H_{17}O$, 232.0888; found, 232.0896.

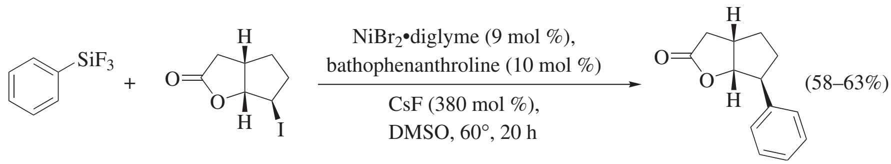


(*E*)-1-(4-Acetyl)phenyl-2-(4-ethoxycarbonyl)phenyl-1-hexene [One-Pot Sequential Heck/Hiyama Coupling Reaction of 2-Pyridylsilanes].[170] To a solution of $Pd(OAc)_2$ (4.3 mg, 0.02 mmol, 10 mol %), tri-2-furylphosphine (5.1 mg, 0.02 mmol, 10 mol %), triethylamine (32.7 mg, 0.32 mmol), and ethyl 4-iodobenzoate (75.2 mg, 0.27 mmol) in THF (0.9 mL) was added (*E*)-dimethyl(2-pyridyl)(1-hexenyl)silane (65.7 mg, 0.30 mmol) under argon, and the reaction mixture was stirred at 60° for 3 h. After the mixture was cooled to rt, 4-iodoacetophenone (48.2 mg, 0.20 mmol) and TBAF (0.46 mmol, 1.0 M in THF) were added to the reaction mixture, and the reaction mixture was stirred at 60° for 14 h. The catalyst was removed by filtration through a short silica gel pad (EtOAc). The filtrate was evaporated, and the residue was chromatographed on silica gel (hexane/EtOAc, 10:1) to afford the product (48.6 mg, 71%) as a colorless oil: IR (neat) 1105, 1271, 1603, 1684, 1717 cm^{-1}; ^1H NMR (300 MHz) δ 0.84 (t, $J = 7.2$ Hz, 3H), 1.27–1.44 (m, 4H), 1.41 (t, $J = 7.2$ Hz, 3H), 2.63 (s, 3H), 2.73 (t, $J = 7.2$ Hz, 2H), 4.40 (q, $J = 7.2$ Hz, 2H), 6.77 (s, 1H), 7.42 (d, $J = 8.7$ Hz, 2H), 7.53 (dm, $J = 8.4$ Hz, 2H), 7.98 (dm, $J = 8.4$ Hz, 2H), 8.06 (dm, $J = 8.7$ Hz, 2H); ^{13}C NMR (75 MHz) δ 13.8, 14.3, 22.6, 26.6, 29.9, 30.7, 60.9, 126.5, 128.4, 128.5, 128.9, 129.4, 129.7, 135.3, 142.7, 144.7, 147.1, 166.4, 197.6; HRMS–EI (m/z): $[M]^+$ calcd for $C_{23}H_{26}O_3$, 350.1882; found, 350.1884.

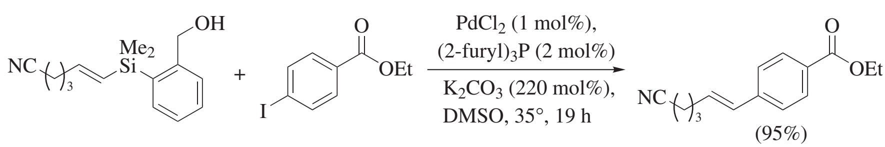


(*E*)-1-(4-Acetylphenyl)-2-nonen-l-one [Palladium-Catalyzed Carbonylative Coupling of an Alkenyltrifluorosilane with an Aryl Iodide].[179] To a THF (1.5 mL) solution of l-(4-iodophenyl)ethanone (49 mg, 0.20 mmol), l-(trifluorosilyl)-l-octene (59 mg, 0.30 mmol), and $[allylPdCl]_2$ (1.8 mg, 2.5 mol %) was added a THF (0.3 mL) solution of TBAF (1.0 M, 0.30 mmol) under 1 atm of carbon monoxide (balloon). After heating at 50° for 10 h, the reaction mixture was cooled to rt, and additional TBAF (0.15 mmol) was introduced. After the mixture was heated at 50° for 12 h, the solvent was removed under reduced pressure to give a crude product. Purification by silica gel column chromatography (hexane/Et_2O, 10:1) afforded l-(4-acetylphenyl)-2-nonen-l-one (44 mg, 85%) as a colorless solid: mp 48–50°; IR (KBr) 2950, 1680, 1620, 1115, 1005, 960, 820 cm^{-1}; ^1H NMR (90 MHz) δ 0.73–1.03 (m, 3H), 1.16–1.80 (m, 8H),

2.07–2.40 (m, 2H), 2.64 (s, 3H), 6.85 (d, J = 17 Hz, 1H), 6.90–7.15 (m, 1H), 8.00 (br s, 4H). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.96; H, 8.61.

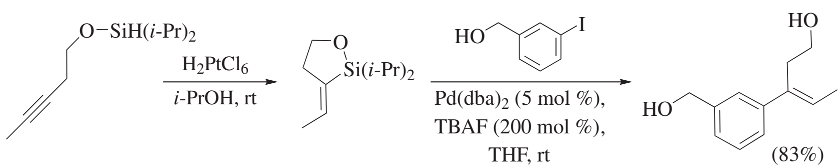


(3a*R,6*R**,6a*S**)-6-Phenylhexahydrocyclopenta[*b*]furan-2-one [Nickel-Catalyzed Cross-Coupling of an Aryltrifluorosilane with a Secondary Alkyl Iodide].[189]** $NiBr_2$•diglyme (23 mg, 0.09 mmol), bathophenanthroline (25 mg, 0.10 mmol), and CsF (574 mg, 3.8 mmol) were added to a 20-mL vial equipped with a stir bar; these compounds were weighed in air, and no special handling precautions were employed. The vial was sealed with a septum screw cap and then evacuated (vacuum pump, 0.5 mmHg) and backfilled with argon (three cycles). DMSO (14.0 mL) was added, and the greenish-yellow suspension was stirred for 10 min. Then phenyltrifluorosilane (1.5 mmol) was added. After the reaction mixture was stirred for an additional 10 min, the alkyl halide (1.0 mmol) was added, and the mixture was heated in an oil bath at 60° for 20 h, with vigorous stirring. The vial was kept sealed during heating and was not attached to an argon or nitrogen inlet. When the reaction was complete, the cooled reaction mixture was poured into Et_2O (50 mL) and filtered through a pad of silica gel, which was washed with Et_2O (3 × 40 mL). The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes/EtOAc, 80:20) to afford the product (117–127 mg, 58-63%) as a colorless oil: R_f 0.15 (hexanes/EtOAc, 80:20); IR (thin film) 2958, 1772 (br), 1495, 1452, 1164, 1036 cm^{-1}; ^1H NMR 300 MHz, $CDCl_3$) δ 1.52–1.66 (m, 1H), 1.78–1.90 (m, 1H), 2.21–2.31 (m, 2H), 2.42 (dd, J = 18.0 Hz, J = 3.0 Hz, H(3), 1H), 2.83 (dd, J = 18.0 Hz, J = 10.0 Hz, H(3), 1H), 2.93–3.05 (m, H(3a), 1H), 3.33 (ddd, J = 10.0 Hz, J = 6.5 Hz, J = 4.0 Hz, H(6), 1H), 4.92 (dd, J = 7.5 Hz, J = 4.0 Hz, H(6a), 1H), 7.23–7.27 (m, 3H), 7.31–7.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.0, 32.6, 35.6, 38.5, 51.9, 91.6, 126.6, 127.0, 128.6, 141.5, 177.1; HRMS–EI (m/z): $[M]^+$ ca1cd for $C_{13}H_{14}O_2$, 202.0994; found, 202.0985.



(*E*)-6-(4-Ethoxycarbonylphenyl)-5-hexenenitrile [Brønsted Base Activated Coupling of a 2-Hydroxymethylphenylsilane].[151] To a mixture of K_2CO_3 (304 mg, 2.2 mmol), tri(2-furyl)phosphine (4.6 mg, 20 μmol), and $PdCl_2$ (1.8 mg, 10 μmol) in DMSO (2.5 mL) were added the alkenylsilane (1.1 mmol)

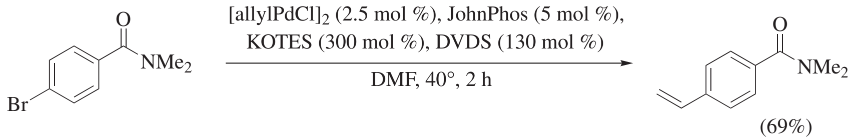
and ethyl 4-iodobenzoate (1.0 mmol) sequentially, and the resulting mixture was stirred at 35°. After 19 h, the mixture was diluted with Et_2O, washed with water and brine, and dried over anhydrous $MgSO_4$. Concentration in vacuo followed by flash chromatography on silica gel afforded the title product (95% yield) as a colorless oil: R_f 0.30 (hexanes/EtOAc, 5:1); IR (neat) 2984, 2937, 2907, 2243, 1711, 1607, 1458, 1437, 1414, 1366, 1271, 1180, 1126, 1109, 1092, 1024, 968, 955, 768, 750, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 3H), 1.86 (m, 4H), 2.38–2.44 (m, 4H), 4.36 (q, J = 7.2 Hz, 2H), 6.22–6.31 (m, 1H), 6.50 (d, J = 16.0 Hz, 1H), 7.39 (d, J = 6.8 Hz, 2H), 7.98 (d, J = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3, 16.5, 24.8, 31.7, 60.9, 119.4, 125.9, 129.1, 129.9, 130.4, 131.2, 141.4, 166.4; EIMS (70 eV) m/z (%) 244 (14, M^+ + 1), 243 (81, M^+), 199 (15), 198 (100), 197 (16), 196 (19), 170 (12), 157 (14), 145 (15), 130 (14), 129 (43), 128 (22), 117 (57), 116 (16), 115 (40); HRMS–EI (70 eV) (m/z): $[M]^+$ calcd for $C_{15}H_{17}NO_2$, 243.1259; found, 243.1259.



(E)-3-(3-Hydroxymethylphenyl)-3-penten-1-ol [Sequential Intramolecular Hydrosilylation/Cross-Coupling of a Homopropargyl Ether].[224] To a solution of diisopropyl-(3-pentynyloxy)silane (10.2 g, 51.5 mmol) in 200 mL of dry CH_2Cl_2 at rt was added H_2PtCl_2•$6H_2O$ (0.90 mL of 0.2 M solution in isopropyl alcohol, 0.18 mmol, 0.35% equiv). A vigorous exotherm was noted; the reaction mixture was cooled in a water bath, and stirring was continued for 70 min. The solvent was then evaporated in vacuo to give 10.7 g of an amber liquid. Fractional distillation of the liquid afforded the cyclic siloxane (8.50 g, 83%) as a colorless liquid: bp 57° (0.5 mm Hg); TLC R_f 0.74 (pentane/Et_2O, 4:1, SiO_2); GC t_R 5.56 min (100%) (HP-5, injector 225°, column 300°, 15 psi); IR (neat) 2941, 2865, 1643, 1463, 1053, 1022 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (m, HC(8), H_3C(9), 14H), 1.77 (md, J = 6.6 Hz, H_3C(7), 3H), 2.47 (m, H_2C(4), 2H), 4.00 (t, J = 6.6 Hz, H_2C(5), 2H), 5.93 (m, HC(6), 1H); ^{13}C NMR: (125.6 MHz, $CDCl_3$) δ 12.6 (C7), 16.8 (C8), 17.2/17.3 (C9′/C9), 32.5 (C4), 67.2 (C5), 133.5 (C6), 136.8 (C3); EIMS (70 eV) m/z (%): 198 (10, M^+), 173 (15), 155 (100), 127 (60), 105 (26), 77 (45). Anal. Calcd for $C_{11}H_{22}OSi$: C, 66.60; H, 11.18; Si, 14.16. Found: C, 66.38; H, 11.29; Si, 14.28.

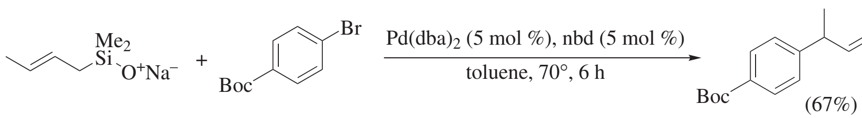
In a two-necked flask fitted with a rubber septum and gas inlet tube, the oxasilacyclopentane (248 mg, 1.25 mmol, 1.1 equiv) was dissolved in a solution of TBAF in THF (2.3 mL, 2.3 mmol, 2.0 equiv), and the mixture was stirred for 10 min at ambient temperature under nitrogen. 2-Iodobenzyl alcohol (264 mg, 1.13 mmol, 1.0 equiv) was added in three portions over 25-min intervals, and $Pd(dba)_2$ (32.4 mg, 0.0565 mmol, 0.050 equiv) was added following the first

portion of iodide. The mixture was stirred at rt for a total of 5 h. The crude mixture was then loaded onto 2 g of silica gel and was purified by column chromatography (SiO_2, 31 g, pentane/Et_2O, 9:7 to 1:1). Removal of the solvent and Kugelrohr distillation of the resulting oil afforded the title product (176 mg, 81%) as a colorless oil: bp 220° (air bath (0.08 mm Hg)); TLC R_f 0.32 (Et_2O, SiO_2); GC t_R 5.59 min (100%) (HP-5, injector 225°, detector 300°, column 270°, 15 psi); IR ($CHCl_3$) 3611 (s), 3012 (s), 2961 (m), 2937 (m), 2884 (m), 1603 (w), 1401 (s), 1384 (m), 1233 (m), 1016 (s), 908 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (br s, OH, 1H), 1.86 (d, $J = 7.1$ Hz, $H_3C(5)$, 3H), 2.84 (t, $H_2C(2)$, 2H), 3.64 (t, $J = 6.9$ Hz, $H_2C(1)$, 2H), 4.69 (s, $H_2C(7')$, 2H), 5.94 (q, $J = 6.9$ Hz, HC(4), 1H), 7.23–7.31 (m, HC(4′), HC(5′), HC(6′), 3H), 7.36 (s, HC(2′), 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 14.6 (C5), 33.0 (C2), 61.4 (C1), 65.6 (C7′), 125.1, 125.7, 125.8, 126.3, 128.8, 136.9, 141.2, 143.3; EIMS (70 eV) m/z (%): 192 (25, M^+), 174 (22), 156 (43), 143 (85), 129 (100), 117 (62), 103 (22), 91 (85), 77 (40). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.89; H, 8.15.

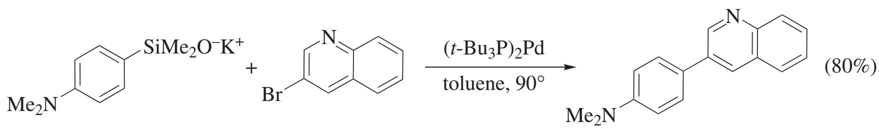


***N,N*-Dimethyl-4-ethenylbenzamide [Base-Promoted Vinylation of an Aryl Bromide with DVDS].**[262] To an oven-dried, 2-necked, 10-mL round-bottomed flask equipped with a magnetic stir bar, septum, and gas adapter was added allylpalladium chloride dimer (18 mg, 0.05 mmol, 0.025 equiv), and 2-(di-*tert*-butylphosphino)biphenyl (29 mg, 0.1 mmol, 0.05 equiv). The gas adapter was attached to an argon manifold, then evacuated and refilled with argon. After this evacuation/refill process was repeated two additional times, the flask was charged with DMF (2 mL) via syringe. The argon adapter was removed, and *N*,*N*-dimethyl-4-bromobenzamide (456 mg, 2 mmol) was quickly added as a solid, and the gas adapter was replaced. To the mixture was added DVDS (597 μL, 2.6 mmol, 1.3 equiv) neat, via syringe. The argon adapter was again removed, KOTES (1 g, 6.0 mmol, 3.0 equiv) was quickly added, and the argon adapter was replaced. An additional 2 mL of DMF was then added via syringe, and the mixture was placed in a preheated oil bath, warmed to 40°, and stirred for 2 h. After the reaction was determined to be complete by GC analysis, the mixture was cooled to rt, and then was partitioned between EtOAc (50 mL) and water (50 mL). The aqueous layer was extracted with EtOAc (50 mL), and the organic layers were washed with water (50 mL). The organic phases were combined, dried over Na_2SO_4, and then were filtered and concentrated in vacuo (rt, 50 mm Hg). Purification of the crude product by column chromatography (silica gel, 30 mm x 120 mm, hexane/EtOAc, 3/2) afforded the product (242 mg, 69%) as a white solid: mp 48–50°; TLC R_f 0.2 (SiO_2, hexane/EtOAc, 3:2); IR 2930 (m), 1653 (m), 1616 (s), 1559 (w), 1517 (w), 1490 (m), 1448 (w), 1395 (s), 1265 (m),

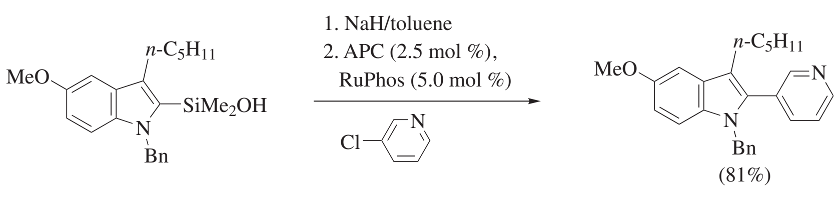
1219 (w), 1180 (w), 1083 (m), 1016 (w), 998 (w), 939 (w), 920 (w), 852 (m), 775 (w), 734 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.98 (s, HC(8), 3H), 3.10 (s, HC(8), 3H), 5.30 (d, J = 10.9, $H_{cis}C(1)$, 1H), 5.79 (d, J = 17.6, $H_{trans}C(1)$, 1H), 6.71 (dd, J = 17.6, J = 10.9, HC(2), 1H), 7.38 (d, J = 8.3, HC(5), 2H), 7.42 (d, J = 8.3, HC(4), 2H); ^{13}C NMR (125 MHz, ($CDCl_3$) δ 35.6 (C8), 39.8 (C8), 115.38 (C1), 126.3 (C4), 127.7 (C5), 135.8 (C6), 136.4 (C2), 139.0 (C3), 171.62 (C7); EIMS (70 eV) m/z (%): 175 (29, M^+), 174 (25), 132 (12), 131 (100), 105 (18), 103 (28), 77 (32).



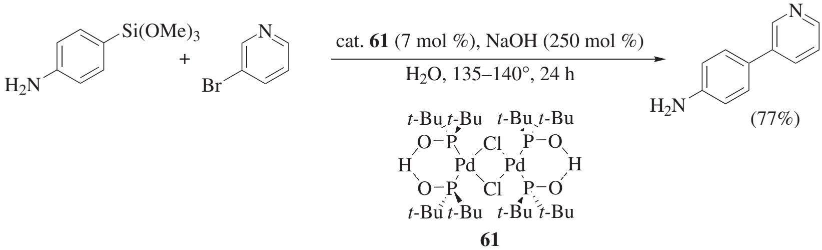
4-(1-Methyl-2-propen-1-yl)benzoic Acid, 1,1-Dimethylethyl Ester [Self-Activated Cross-Coupling of Sodium 2-Butenyltrimethylsilanolate with an Aryl Bromide].[108] To an oven-dried, single-neck, 5-mL round-bottomed flask containing a magnetic stir bar, equipped with a reflux condenser and an argon inlet capped with a septum, was added $Pd(dba)_2$ (28.8 mg, 0.05 mmol, 0.05 equiv). The flask was then sequentially evacuated and filled with argon three times. Then *tert*-butyl 4-bromobenzoate (257 mg, 1.0 mmol) was added by syringe. Sodium 2-butenyldimethylsilanolate (308 mg, 2.0 mmol, 2.0 equiv), pre-weighed into a 10-mL, two-necked round-bottomed flask in a drybox, was dissolved in toluene (2.0 mL), and then norbornadiene (nbd, 5.2 μL, 0.05 mmol, 0.050 equiv) was added by syringe. The solution of the silanolate and nbd in toluene was added to the aryl bromide by syringe. The reaction mixture was heated under argon to 70° in a preheated oil bath. After 6 h, the mixture was cooled to rt, filtered through silica gel (2 cm x 2 cm) in a glass-fritted filter (coarse, 2 cm x 5 cm), and the filter cake washed with Et_2O (3 × 10 mL). The filtrate was concentrated (rt, 20 mm Hg) and the residue was purified by silica gel chromatography (20 cm x 20 mm, hexane/EtOAc, gradient 100:0 to 20:1), followed by Kugelrohr distillation, to afford the product (155 mg, 67%) as a clear, colorless oil: bp 155° (5 mmHg, ABT); TLC R_f 0.33 (hexane/EtOAc, 20:1) [silica gel, UV]; GC γ-t_R: 6.70 min, α-t_R: 6.88 and 6.95 min (25:1 [3.2:1], γ:α [(E) or (Z)]) IR (film) 2975 (m), 2931 (m), 1718 (s), 1700 (m), 1636 (w), 1610 (m), 1578 (w), 1507 (w), 1477 (m), 1457 (m), 1413 (m), 1392 (m), 1368 (m), 1291 (s), 1256 (m), 1167 (m), 1117 (m), 1017 (m), 915 (m), 849 (m), 771 (m), 708 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.37 (d, J = 7.0 Hz, HC(5), 3H), 1.59 (s, HC(11), 1H), 3.51 (ap, J = 7.0 Hz, HC(6), 1H), 5.05 (m, HC(8), 2H), 5.98 (ddd, J = 17.7 Hz, J = 9.8 Hz, J = 6.4 Hz, HC(7), 1H), 7.26 (m, HC(2), 2H), 7.93 (m, HC(3), 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.8 (C5), 28.5 (C11), 43.3 (C6), 81.0 (C10), 114.0 (C8), 127.4 (C2), 129.9 (C3), 130.2 (C4), 142.7 (C7), 150.6 (C1), 166.0 (C9); EIMS (70 eV) m/z (%): 232 (12, M^+), 176 (48), 159 (53), 131 (100), 117 (37), 84 (18). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.28; H, 8.72.



3-(4-*N,N*-Dimethylaminophenyl)quinoline [Self-Activated Cross-Coupling of a Potassium Dimethylarylsilanolate with an Aryl Bromide].[54] In an oven-dried, 5-mL, round-bottomed flask equipped with a magnetic stir bar, reflux condenser, and three-way argon adapter was charged $(t\text{-Bu}_3\text{P})_2\text{Pd}$ (12.8 mg, 0.025 mmol, 2.5 mol %) in a drybox. The flask was sealed away from the atmosphere and removed to a hood. Dry toluene (2 mL) was added via syringe through the three-way adapter, resulting in a colorless solution on stirring. 3-Bromoquinoline (136 mL, 1.0 mmol, 1.0 equiv) and potassium (4-dimethyl-aminophenyl)dimethylsilanolate (350 mg, 1.5 mmol, 1.5 equiv) were added sequentially by removal of the adapter, adding the reagents as liquid and solid, respectively, and replacing the adapter as quickly as possible. The flask was placed into a preheated 90° oil bath and stirred at 90° under a static flow of argon. After 3 h, the mixture was cooled to rt and poured onto water (10 mL). The aqueous layer was extracted with EtOAc (3 × 20 mL), and the organic extracts were washed with brine (15 mL) and dried ($MgSO_4$, 5 g). Purification by MPLC (24 g of SiO_2, 30 mL/min, hexane/EtOAc 9:1, 3 CV), gradient to hexane/EtOAc 3:2 (5 CV), hexane/EtOAc 3:2 (6 CV)), followed by sublimation (80°, 0.1 mmHg), afforded analytically pure yellow-colored plates (198 mg, 80%): mp 127–129°; TLC R_f 0.26 (SiO_2, hexanes/EtOAc, 3:2); IR (KBr) 2952 (w), 2849 (w), 2798 (w), 1602 (s), 1525 (s), 1355 (m), 1292 (w), 1212 (m), 1061 (w), 950 (w), 813 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.03 (s, $H_3C(5')$, 6H), 6.86 (d, $J = 8.9$ Hz, HC(3′), 2H), 7.54 (ddd, $J_1 = 1.4$ Hz, $J_2 = 7.0$ Hz, $J_3 = 8.3$ Hz, HC(5), 1H), 7.64 (d, $J = 8.9$ Hz, HC(2′), 2H), 7.67 (ddd, $J_1 = 1.4$ Hz, $J_2 = 7.0$ Hz, $J_3 = 8.3$ Hz, HC(4), 1H), 7.84 (d, $J = 8.4$ Hz, HC(6), 1H), 8.11 (d, $J = 8.4$ Hz, HC(3), 1H), 8.22 (d, $J = 2.2$ Hz, HC(7), 1H), 9.19 (d, $J = 2.2$ Hz, HC(2), 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 40.4 (C5′), 40.5 (C5′), 112.8 (C3′), 125.4 (C9), 126.7 (C5), 127.7 (C6), 128.0 (C2′), 128.3 (C1), 128.6 (C4), 129.1 (C3), 131.3 (C7), 133.8 (C4′), 146.7 (C8), 149.9 (C2), 150.4 (C1′); EIMS (70 eV) m/z (%): 248 (M^+, 100), 232 (12), 218 (1), 204 (12), 176 (4), 151 (2), 124 (10), 102 (6), 88 (4); HRMS (m/z): $[M]^+$ calcd $C_{17}H_{16}N_2$, 248.1314; found, 248.1312. Anal. Calcd for $C_{18}H_{20}O_3$: C, 82.22; H, 6.49; N, 11.28. Found: C, 81.88; H, 6.46; N, 11.23.



1-Benzyl-5-methoxy-3-pentyl-2-(pyridin-3-yl)-1*H*-indole [Brønsted Base Promoted Cross-Coupling of an Indolylsilanol with an Aryl Chloride].[209] To a flame-dried, 5-mL round-bottomed flask equipped with a stir bar was added NaH (29 mg, 1.2 mmol, 1.2 equiv) and toluene (0.4 mL) under dry argon atmosphere inside a drybox. In a separate flame-dried 5-mL conical flask was added *N*-benzyl-5-methoxy-3-pentyl-(2-indolyl)dimethylsilanol (458 mg, 1.2 mmol, 1.2 equiv) in toluene (2.0 mL); this silanol solution was added dropwise to the above suspension by glass pipette. The conical flask containing the silanol was washed with toluene (0.4 mL), and the rinse was added to the reaction mixture. The resulting mixture was stirred for 10 min whereupon 3-chloropyridine (95 mL, 1.0 mmol, 1.0 equiv), RuPhos (23 mg, 0.05 mmol, 0.05 equiv), and APC (9 mg, 0.025 mmol, 0.025 equiv) were added. The flask was sealed with a rubber septum and removed from the drybox. After being stirred at 70° for 1 h, the black, crude reaction mixture was filtered through a plug of silica gel (3 g), which was eluted with EtOAc (200 mL) to give a light-yellow solution that was concentrated under reduced pressure. The resulting yellow semi-solid was purified by silica gel column chromatography (20 × 100 mm) and eluted with hexane/EtOAc 4:1 (30 × 10-mL fractions). The combined fractions were further purified by concentration and recrystallization in boiling hexane (2 mL) to afford the product (312 mg, 81%) as light-yellow plates: mp 101–102° (hexane); TLC R_f 0.09 (SiO_2, hexane/EtOAc, 4:1) [silica gel, UV]; IR (Nujol) 3057 (w), 3026 (w), 2958 (s), 2940 (s), 2911 (s), 2857 (s), 1612 (w), 1581 (w), 1568 (w), 1543 (w), 1496 (w), 1484 (m), 1468 (s), 1453 (s), 1424 (m), 1377 (m), 1351 (m), 1223 (m), 1181 (m), 1169 (m), 1100 (w), 1043 (m), 1029 (m), 1021 (m), 832 (m), 810 (s), 718 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, J = 6.8 Hz, HC(5‴), 3H), 1.26 (m, HC(3‴), HC(4‴), 4H), 1.62 (m, HC(2‴), 2H), 2.66 (t, J = 7.6 Hz, HC(1‴), 2H), 3.90 (s, HC(10), 3H), 5.16 (s, HC(1′), 2H), 6.86 (m, HC(3′), HC(6), 3H), 7.11 (m, HC(7), HC(4), 2H), 7.23 (m, HC(5′), HC(4′), 3H), 7.31 (dd, J = 7.8 Hz, J = 4.9 Hz, HC(5″), 1H), 7.56 (dt, J = 7.8 Hz, J = 2.0 Hz, HC(6″), 1H), 8.58 (d, J = 1.8 Hz, HC(2″), 1H), 8.61 (dd, J = 4.9 Hz, J = 1.7 Hz, HC(4″), 1H); ^{13}C NMR (125.6 MHz, $CDCl_3$) δ 14.0 (C5‴), 22.4 (C4‴), 24.5 (C1‴), 30.6 (C2‴), 31.7 (C3‴), 47.6 (C1′), 55.9 (C10), 101.4 (C4), 111.0 (C7), 112.2 (C6), 115.6 (C3), 123.1 (C5″), 125.8 (C3′), 127.2 (C5′), 128.2 (C2), 128.3 (C2′), 128.6 (C4′), 132.5 (C1″), 134.5 (C9), 137.6 (C6″), 138.1 (C8), 149.1 (C2″), 151.0 (C4″), 154.1 (C5); EIMS (70 eV) m/z (%): 384 (55, M^+), 327 (100), 277 (10), 193 (7), 91 (92). Anal. Calcd for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29. Found: C, 80.92; H, 7.42; N, 7.24.



4-(3-Pyridyl)aniline [Cross-Coupling of an Aryltrialkoxysilane with an Aryl Bromide in Aqueous NaOH].[245] A mixture of 3-bromopyridine, (100 mg), catalyst **61** (7 mol %), and 4-aminophenyltrimethoxysilane (2 equiv) was stirred in 5 mL of 0.5 M aqueous NaOH at 135° for 24 h using a closed vessel. The reaction mixture was allowed to cool to rt, and then was quenched with water and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvents were removed under vacuum. The residue was purified by flash chromatography on silica gel (hexanes/EtOAc/Et_3N, 100:10:1) to afford the coupling product (77%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (bs, 2H), 6.76 (d, $J = 8.5$ Hz, 2H), 7.30 (dd, $J = 5.0$ Hz, $J = 8.0$ Hz, 1H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.79 (ddd, $J = 2.2$ Hz, $J = 2.2$ Hz, $J = 8.0$ Hz, 1H), 8.47 (d, $J = 5.0$ Hz, 1H), 8.77 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 115.7, 123.7, 127.8, 128.2, 133.8, 136.9, 146.9, 147.1, 147.5; EIMS (70 eV) m/z (%): 169 (100, M^+–H), 142 (14, M^+–H,–HCN), 117 (9, M^+–HCN,–C_2H_2).

TABULAR SURVEY

The tables are organized by the structure of the transferable group attached to silicon and the structure of the electrophile. Thus, the primary rubric of the tables follows the order: arylsilanes (Table 1), heteroarylsilanes (Table 2), alkenylsilanes (Table 3), alkynylsilanes (Table 4), sp^3 (i.e. alkyl) silanes (Table 5) and acylsilanes (Table 6). Table 7 contains oxidative Heck reactions for completeness. Carbons attached to the transferable group through heteroatoms are not counted. The secondary rubric (i.e. A, B, C, etc.) follows the order: aryl electrophiles, heteroaryl electrophiles, alkenyl electrophiles, alkynyl electrophiles, allyl electrophiles, and alkyl electrophiles. This organization is intentionally different from that in the "Scope and Limitations" section to allow the reader to make direct comparisons of substrate types independent of the nature of the silicon donor group. Although this organization allows the reader to identify which silicon moiety would be most suitable for a given pair of transferable group and electrophile, a hierarchy for presenting the various silicon groups had to be constructed that would be consistent across all tables. The hierarchy proceeds as follows: (1) increasing number of heteroatoms on silicon, (2) total carbon count of carbon moieties bonded to silicon, (3) atomic number of substituents on silicon, and (4) carbon count of heteroatomic substituents bonded to silicon. A graphical illustration of that hierarchy is found in Figure 5.

A series of charts precedes the tables. These charts depict catalysts, ligands, and reagents that are indicated by bold numbers in the table entries, and are arranged primarily by structural type. The reader is referred to these charts to locate the structure with which the bold numbers are associated.

The tables cover the literature through 2008.

The following abbreviations are used in the tables:

Bphen	1,10-phenanthroline
$Cy_3P(O)$	tricyclohexylphosphine oxide

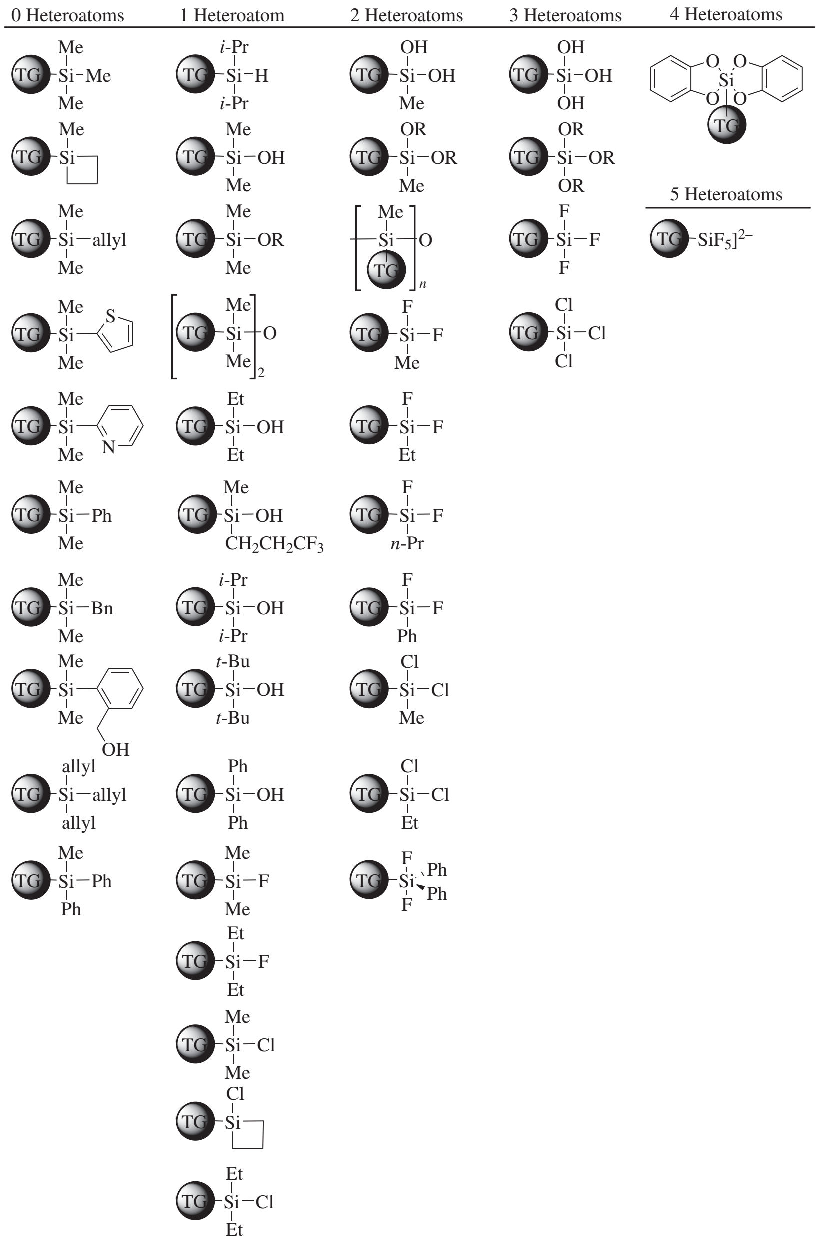


Figure 5. Hierarchy of silicon groups for the third rubric in the tables.

dCypb	1,4-(dicyclohexylphosphino)butane
(−)-DIOP	1,1′-[[(4*R*, 5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl]bis(methylene)]bis[1,1-diphenyphosphine]
DMI	1,3-dimethyl-2-imidazolidinone
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DVDS	divinyltetramethylsiloxane
glyme	1,2-dimethoxyethane
MW	microwave irradiation
NaHMDS	sodium bis(trimethylsilyl)amide
nbd	norbornadiene
PEG	polyethylene glycol
SCS	sodium dodecyl sulfate
TBAB	tetra-*n*-butylammonium bromide
TBAC	tetra-*n*-butylammonium chloride
TBAT	tetra-*n*-butylammonium difluorotriphenylsiliconate
TBOH	tetra-*n*-butylammonium hydroxide

CHART 1. LIGANDS USED IN TABLES

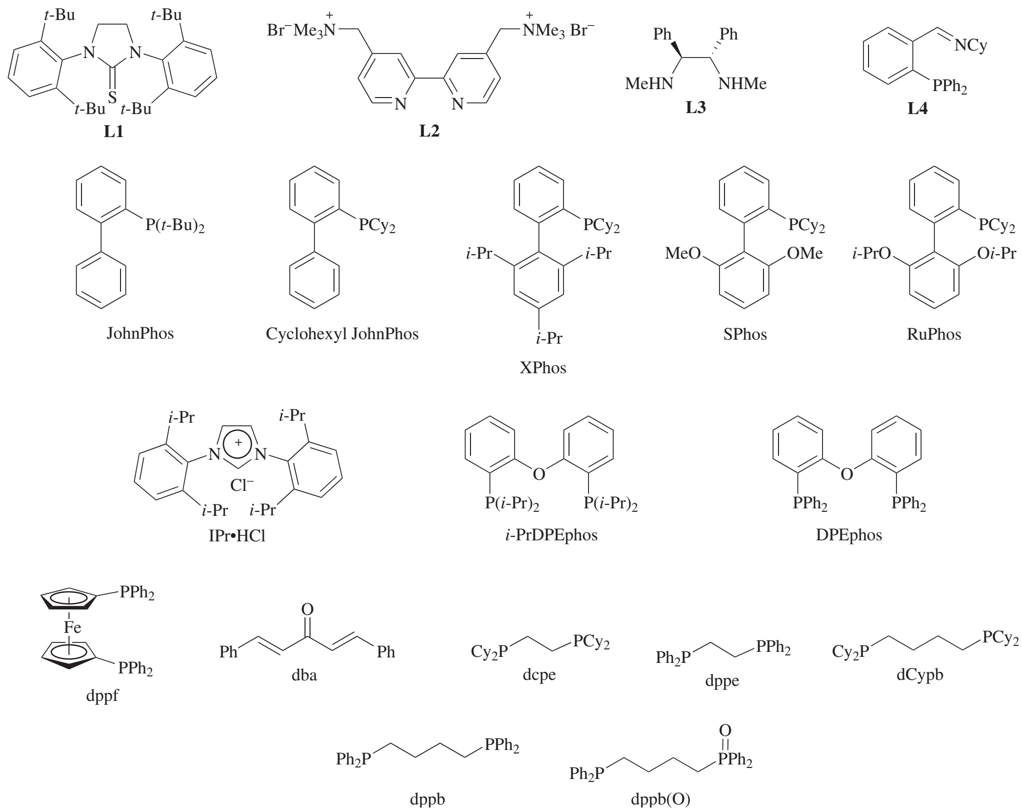
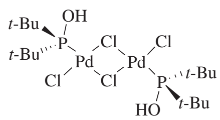


CHART 2. PALLADIUM CATALYSTS USED IN TABLES



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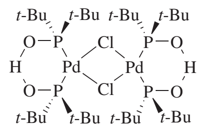

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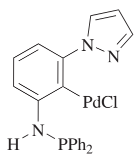

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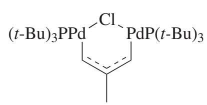

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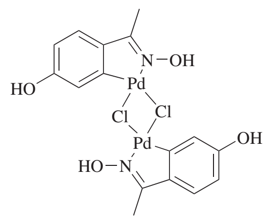

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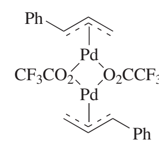
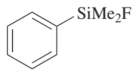
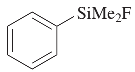
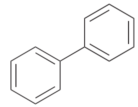
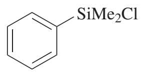
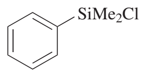
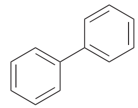
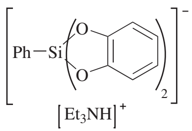
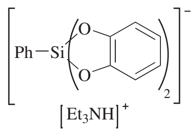
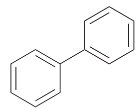
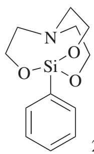
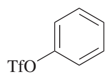
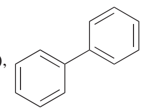
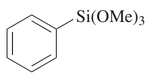
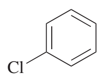
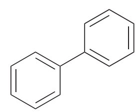
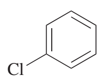
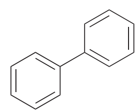


Pd cat. **6**

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		CuI (5%), TBAF (120%), MeCN, rt, 5 min	 (76)	178
		CuI (5%), TBAF (120%), MeCN, rt, 5 min	 (73)	178
		$Pd(PPh_3)_4$ (5%), dioxane, reflux, 60 h	 (75)	87
 200%		$Pd(dba)_2$ (10%), Cyclohexyl JohnPhos (20%), TBAF•$3H_2O$ (200%), H_2O (2000%), THF, reflux, 12 h	 (75)	260
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (31)	237
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), acetone, 80°, 24 h	 (35)	238

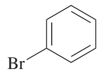
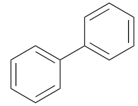
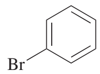
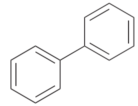
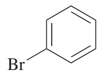
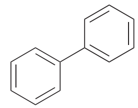
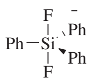
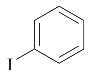
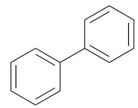
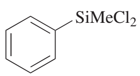
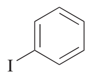
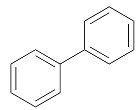
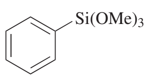
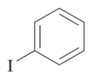
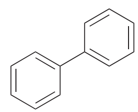
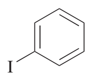
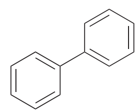
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(96)	237
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(96)	234
400%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (400%), dioxane, 80°, 4 h		(82)	238
 n-Bu_4N^+ 200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 2 h		(85)	270
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h		(100)	186
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(90)	237
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(94)	234

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
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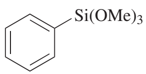
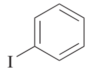
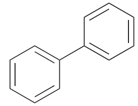
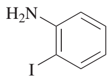
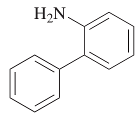
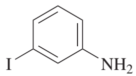
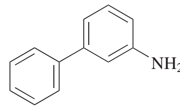
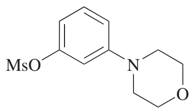
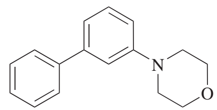
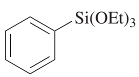
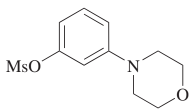
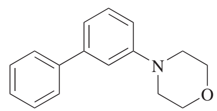
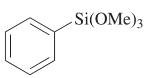
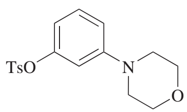
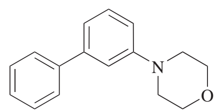
 200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), dioxane, 80°, 1 h	 (86)	238
200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°	 (82)	232
200%		$Pd(OAc)_2$ (10%), P(*o*-tol)$_3$ (20%), TBAF (200%), DMF, 85°	 (75)	232
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 (87)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 (92)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (97)	249

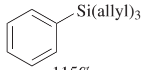
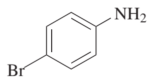
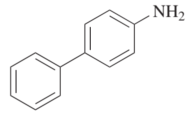
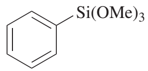
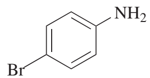
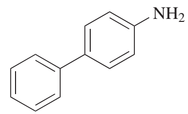
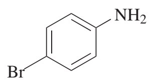
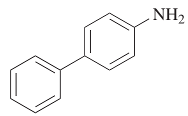
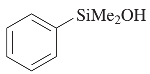
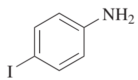
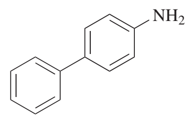
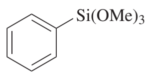
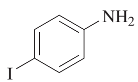
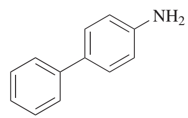
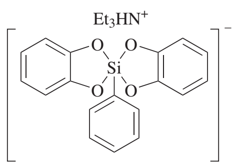
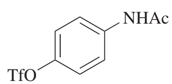
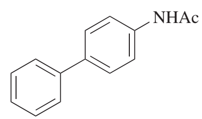
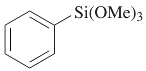
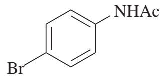
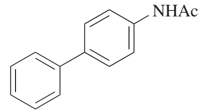
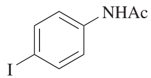
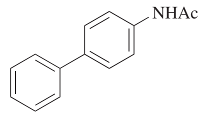
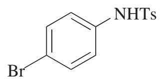
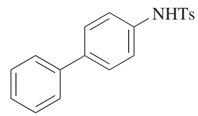
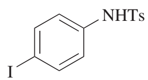
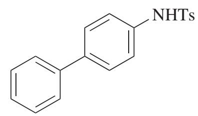
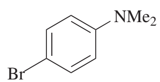
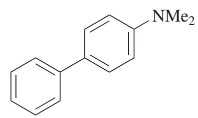
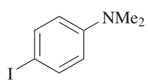
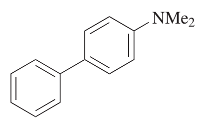
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h		(83)	47
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°		(48)	232
200%		$Pd(OAc)_2$ (10%), P(*o*-tol)$_3$ (20%), TBAF (200%), DMF, 85°		(78)	232
 120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAT (12%), THF, 70°, 0.5 h		(52)	201
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°		(95)	232
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(92)	276

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 200%		$Pd(OAc)_2$ (10%), $P(o\text{-tol})_3$ (20%), TBAF (200%), DMF, 85°		(77)	232
200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°		(70)	232
200%		$Pd(OAc)_2$ (10%), $P(o\text{-tol})_3$ (20%), TBAF (200%), DMF, 85°		(72)	232
200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°		(65)	232
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(87)	237
200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 85°		(69)	232

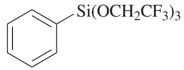
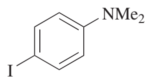
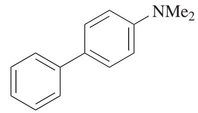
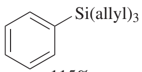
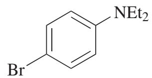
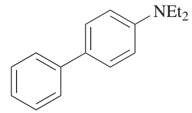
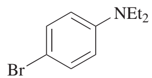
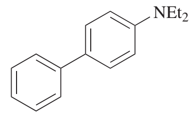
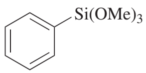
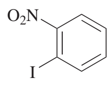
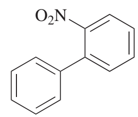
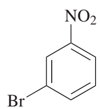
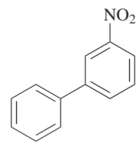
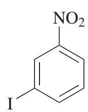
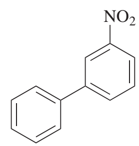
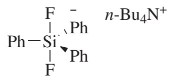
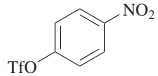
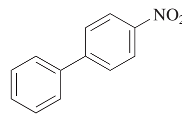
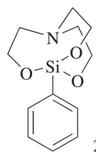
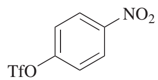
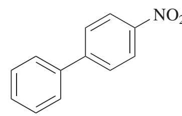
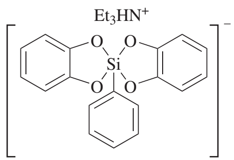
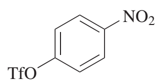
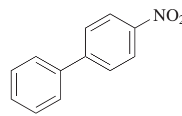
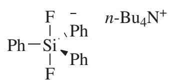
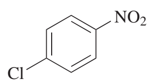
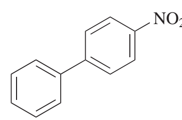
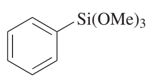
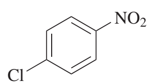
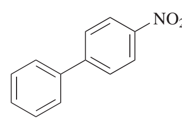
 200%		Pd(OAc)$_2$ (10%), PPh$_3$ (20%), TBAF (200%), DMF, 85°		(85)	232
 115%		TBAF•3H$_2$O (460%), PdCl$_2$ (5%), PCy$_3$ (10%), DMSO/H$_2$O (20:1), 80°, 3 h		(88)	47
110%		1. TBAF (440%), DMSO/H$_2$O (10:1), rt, 1 h 2. PdCl$_2$ (5%), PCy$_3$ (10%), 80°, 5 h		(75)	46
 200%		Pd(OAc)$_2$ (10%), PPh$_3$ (20%), TBAF (200%), DMF, 85°		(58)	232
200%		Pd(OAc)$_2$ (3%), **L1** (12%), TBAF•3H$_2$O (200%), dioxane, 80°, 24 h		(66)	238
120%		Na$_2$PdCl$_4$ (1.5%), SDS (20%), NaOH (600%), H$_2$O, 100°, 5 min		(93)	234

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(dba)_2$ (10 mol%), THF, 95°, 2.5 h	 (73)	69
 200%		$Pd(dba)_2$ (10%), TBAF•$3H_2O$ (200%), PPh_3 (20%), H_2O (1000%), THF, reflux, 2 h	 (50)	260
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (46)	276
 200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 26 h	 (54)	270
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (90)	237

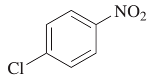
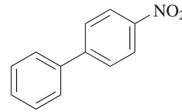
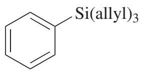
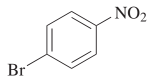
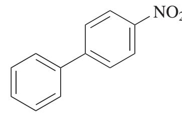
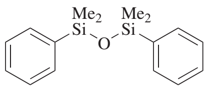
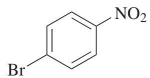
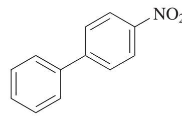
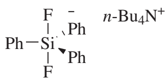
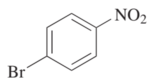
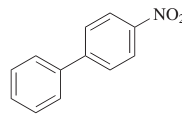
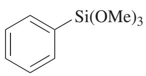
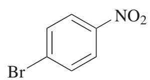
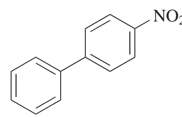
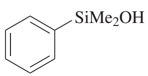
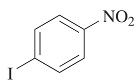
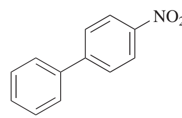
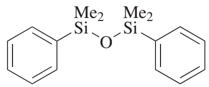
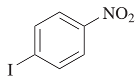
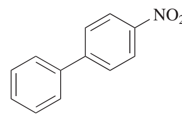
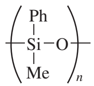
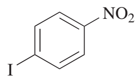
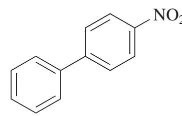
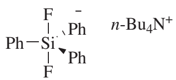
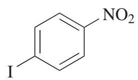
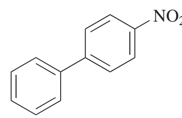
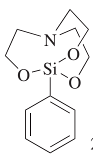
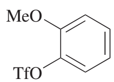
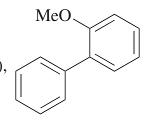
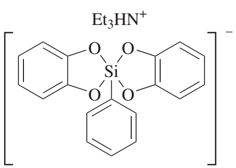
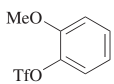
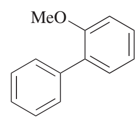
400%		Pd(OAc)$_2$ (3%), **L1** (12%), TBAF•3H$_2$O (400%), dioxane, 80°, 24 h	 (78)	238
 115%		TBAF•3H$_2$O (460%), PdCl$_2$ (5%), PCy$_3$ (10%), DMSO/H$_2$O (10:1), 80°, 4 h	 (87)	47
 150%		Pd(PPh$_3$)$_4$ (5%), Ag$_2$O (100%), TBAT (10%), dioxane, 70°, 1 h	 (92)	201
 200%		[allylPdCl]$_2$ (2.5%), DMSO, 120°, 4 h	 (77)	270
 200%		Pd(OAc)$_2$ (3%), **L1** (12%), TBAF•3H$_2$O (200%), dioxane, 80°, 24 h	 (81)	238
 120%		Pd(PPh$_3$)$_4$ (3%), Ag$_2$O (100%), TBAT (12%), THF, 70°, 0.5 h	 (78)	201

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 1 h	 (85)	201
 1 mmol per unit	 0.2 mmol	$Pd(PPh_3)_3$ (5%), Ag_2O (100%), THF, 60°, 24 h	 (96)	268
 200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 1.5 h	 (89)	270
 200%		$Pd(dba)_2$ (10%), Cyclohexyl JohnPhos (20%), TBAF•$3H_2O$ (200%), H_2O (2000%), THF, reflux, 12 h	 (90)	260
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (95)	276

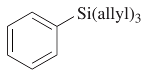
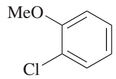
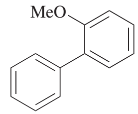
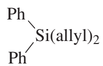
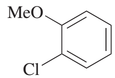
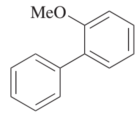
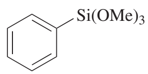
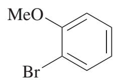
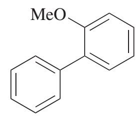
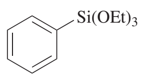
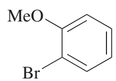
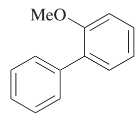
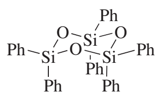
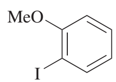
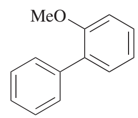
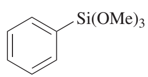
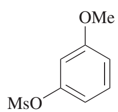
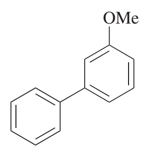
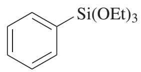
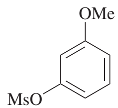
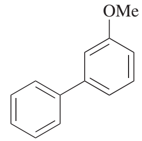
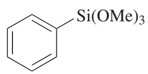
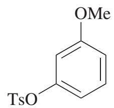
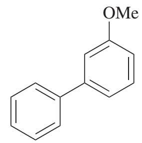
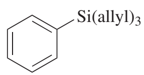
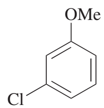
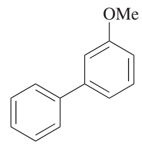
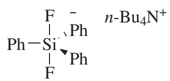
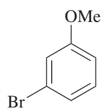
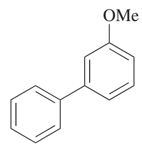
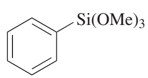
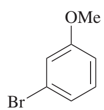
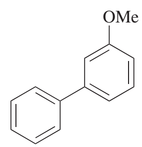
 125%		TBAF•3H_2O (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h		(94)	47
 150%		TBAF•3H_2O (600%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (25:1), 80°, 12 h		(79)	47
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(90)	234
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 3 h		(46)	246
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1: 1), reflux, 4 h		(87)	265
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH, 90°		(94)	248

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 (97)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (85)	249
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h	 (99)	47
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1) 135–140°, 24 h	 (73)	269
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (87)	237

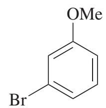
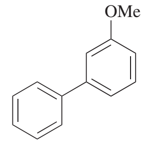
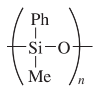
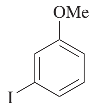
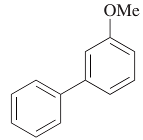
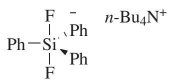
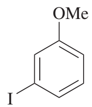
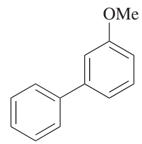
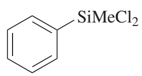
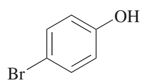
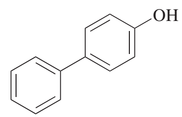
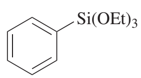
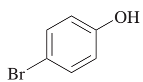
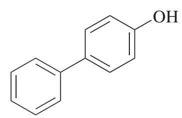
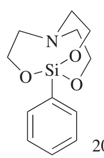
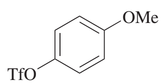
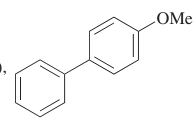
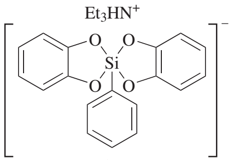
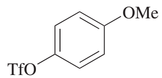
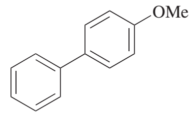
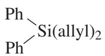
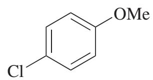
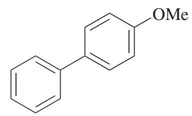
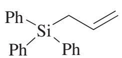
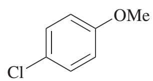
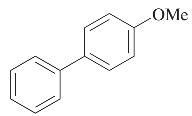
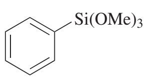
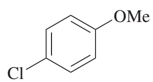
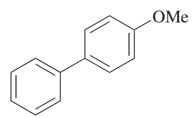
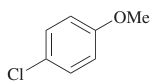
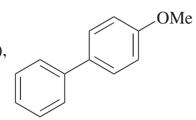
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(90)	234
 1 mmol per unit	 0.2 mmol	$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 24 h		(59)	268
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(87)	269
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h		(59)	186
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 24 h		(78)	246
 200%		$Pd(dba)_2$ (10%), Cyclohexyl JohnPhos (20%), TBAF•$3H_2O$ (200%), H_2O (2000%), THF, reflux, 12 h		(90)	260

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (96)	276
 150%		$TBAF•3H_2O$ (600%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (25:1), 80°, 8 h	 (93)	47
 105%		$TBAF•3H_2O$ (330%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (40:1), 80°, 12 h	 (86)	47
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 80°, 45 h	 (29)	236
200%		Pd_2dba_3 (10%), Cyclohexyl JohnPhos (15%), TBAF (200%), DMF, 87°, 27 h	 (71)	236

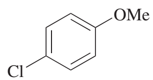
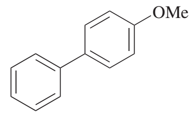
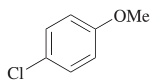
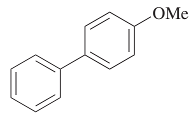
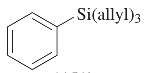
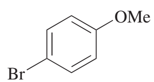
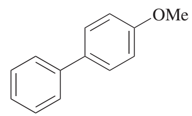
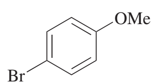
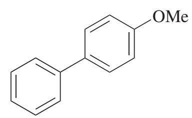
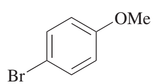
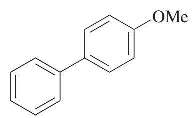
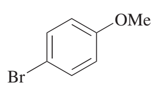
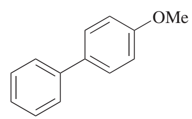
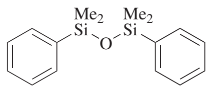
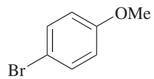
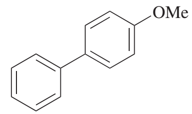
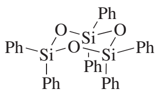
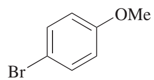
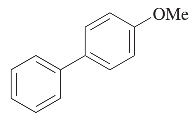
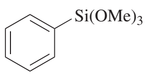
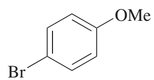
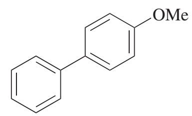
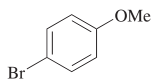
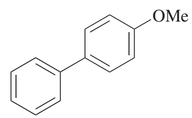
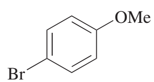
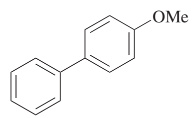
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(11)	237
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (20%), dioxane, 80°, 48 h		(11)	238
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h		(92)	47
125%		TBAF•$3H_2O$ (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(97)	47
110%		1. TBAF•$3H_2O$ (440%), DMSO/H_2O (2:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%) 80°, 6 h		(100)	46
150%		TBAF•$3H_2O$ (600%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (15:1), 80°, 11 h		(93)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAT (10%), dioxane, 70°, 1 h		(31)	201
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 4 h		(91)	265
 200%		$Pd(OAc)_2$ (5%), PPh_3 (10%), TBAF (200%), DMF, 90°, 24 h		(87)	236
200%		$Pd(OAc)_2$ (10%), P(*o*-tol)$_3$ (20%), TBAF (200%), DMF, 90°, 24 h		(70)	236
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(92)	234

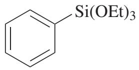
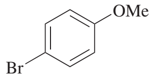
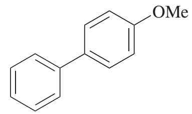
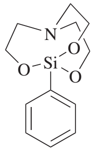
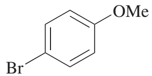
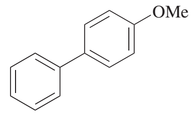
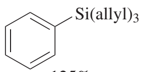
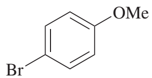
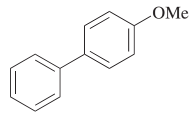
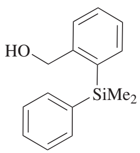
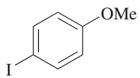
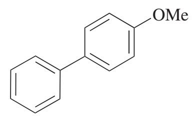
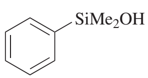
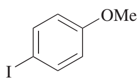
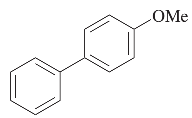
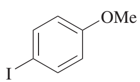
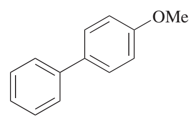
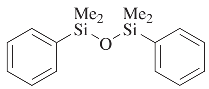
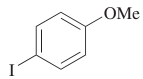
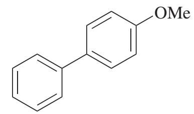
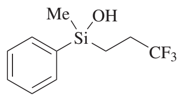
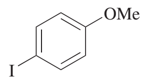
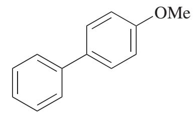
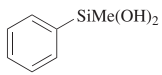
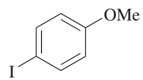
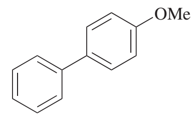
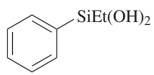
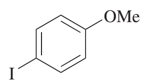
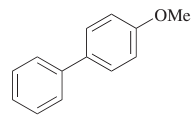
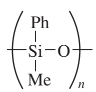
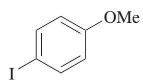
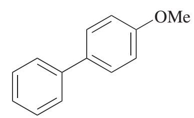
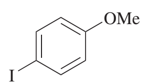
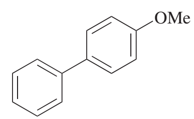
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 24 h		(78)	246
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), THF, reflux, 2 h		(73)	260
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(97)	47
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 16 h		(99)	151
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(35)	37
120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAT (12%), THF, 70°, 0.5 h		(85)	201

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 1 h		(96)	201
 120%		$Pd(OAc)_2$ (5%), Ag_2O (100%), THF, 60°, 7 h		(51)	203
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h		(93)	37
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h		(80)	37
 1 mmol per unit	 0.2 mmol	$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 20 h		(52)	268
		Pd_2dba_3•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 20 h		(79)	268

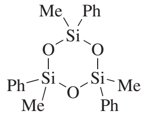
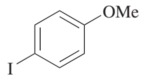
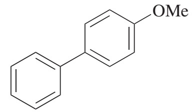
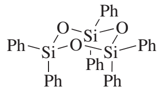
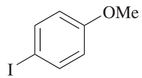
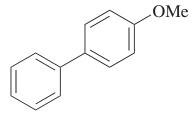
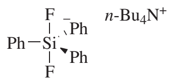
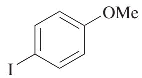
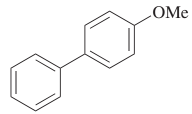
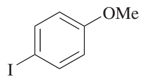
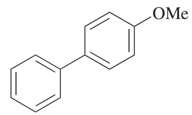
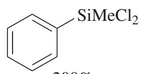
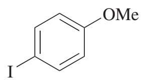
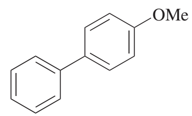
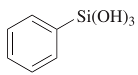
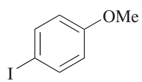
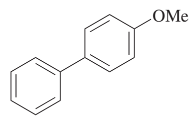
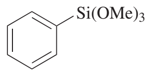
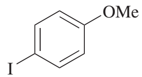
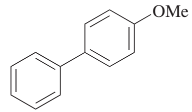
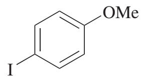
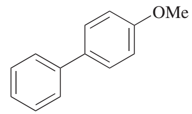
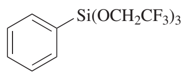
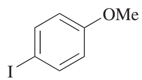
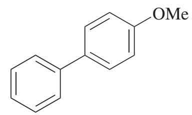
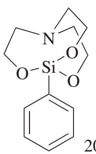
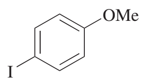
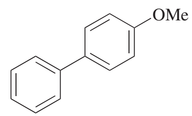
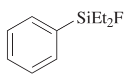
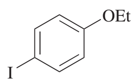
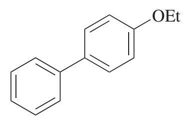
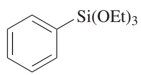
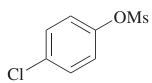
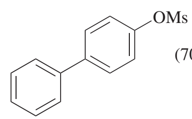
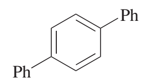
 100%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 120 h		(39)	268
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 4 h		(91)	265
 200%		$[allylPdCl]_2$ (10%), DMF, 95°, 19 h		(97)	69
200%		$Pd(dba)_2$ (10%) THF, 95°, 2.5 h		(88)	69
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h		(80)	186
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h		(83)	37

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 250%		$Pd(dba)_2$ (9%), TBAF (360%), DMF, 95°, 2 h	 (54)	70
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (20%), dioxane, 80°, 1 h	 (95)	238
 190%		$Pd(dba)_2$ (9%), TBAF (190%), DMF, 95°, 2 h	 (77)	70
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), THF, reflux, 2 h	 (78)	260
 120–150%		$[allylPdCl]_2$ (2.5–5.0%), KF (200%), DMF, 70°, 10 h	 (81)	73
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (150%), THF/*t*-BuOH (1:1), 90°	 (70) +  (22)	248

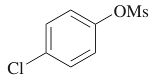
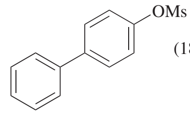
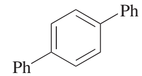
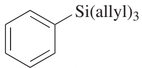
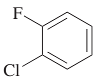
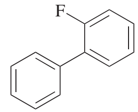
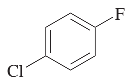
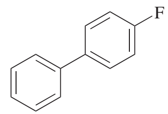
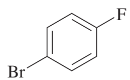
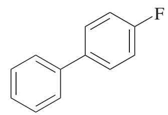
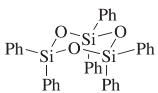
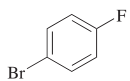
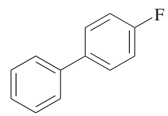
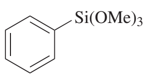
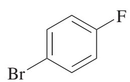
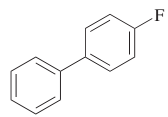
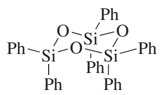
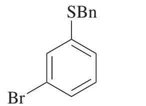
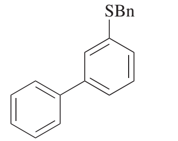
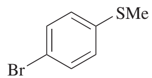
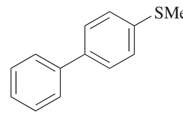
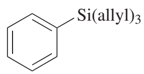
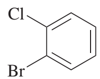
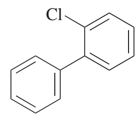
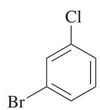
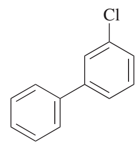
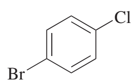
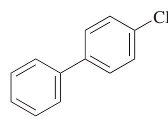
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (300%), THF/*t*-BuOH (1:1), 90°	 (18) +  (68)	248
 125%		$TBAF\bullet3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h	 (85)	47
125%		$TBAF\bullet3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h	 (91)	47
115%		$TBAF\bullet3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), $DMSO/H_2O$ (10:1), 80°, 2 h	 (95)	47
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 2 h	 (85)	265
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (92)	234

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 9 h	 (67)	265
20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 24 h	 (70)	265
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 10 h	 (87)	47
		1. TBAF•$3H_2O$ (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 12 h	 (93)	160
115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 12 h	 (98)	47

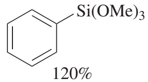
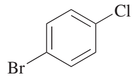
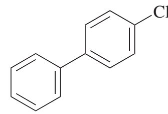
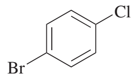
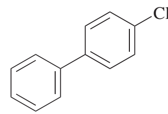
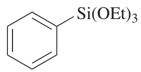
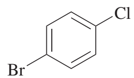
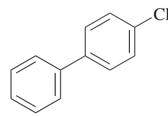
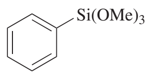
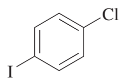
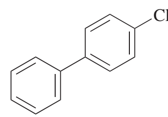
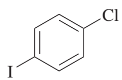
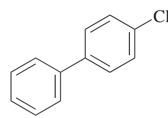
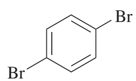
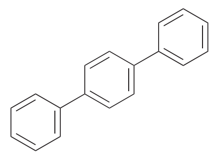
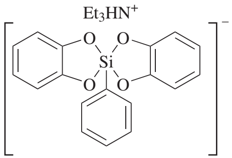
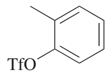
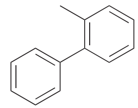
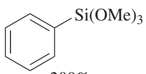
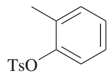
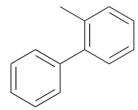
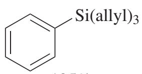
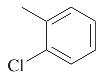
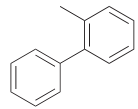
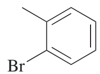
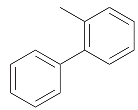
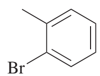
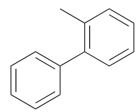
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(94)	234
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), dioxane, 80°, 4 h		(86)	238
 150%		$Pd(NH_3)_2Cl_2$ (0.01%), **L2** (0.01%), NaOH (200%), H_2O, 120°, 36 h		(88)	246
 220%		$Pd(dba)_2$ (9%), TBAF (220%), DMF, 95°, 2 h		(78)	70
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), dioxane, 80°, 2 h		(95)	238
400%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (400%), dioxane, 80°, 6 h		(65)	238

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (92)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (30)	249
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 16 h	 (88)	47
115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h	 (91)	47
150%		TBAF•$3H_2O$ (600%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (15:1), 80°, 14 h	 (87)	47

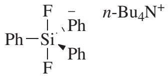
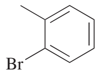
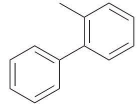
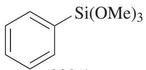
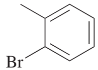
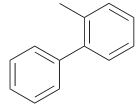
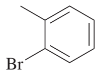
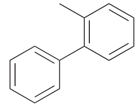
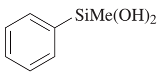
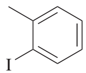
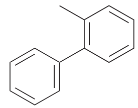
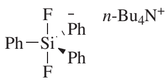
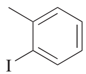
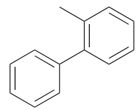
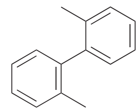
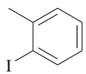
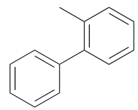
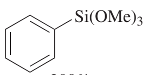
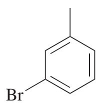
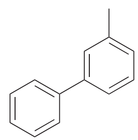
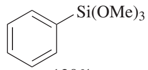
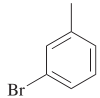
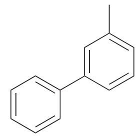
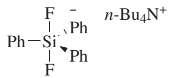
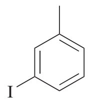
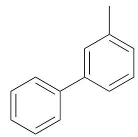
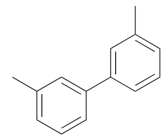
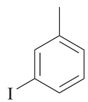
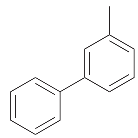
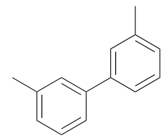
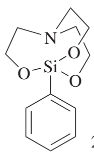
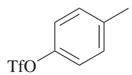
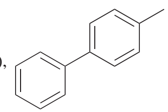
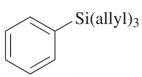
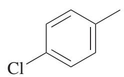
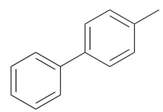
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (67)	269
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (81)	237
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (92)	234
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h	 (84)	37
 140%		[allylPdCl]$_2$ (10%), DMF, 95°, 4 h	 (93) +  (2)	69
200%		$Pd(dba)_2$ (10%), THF, 95°, 5 h	 (90)	69
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (90)	237

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (86)	234
 140%		$[allylPdCl]_2$ (10%), DMF, 95°, 24 h	 (97) +  (3)	69
200%		$Pd(dba)_2$ (10%), THF, 95°, 26.5 h	 (68) +  (10)	69
 200%		$Pd(dba)_2$ (10%), Cyclohexyl JohnPhos (20%), TBAF•$3H_2O$ (200%), H_2O (2000%), THF, reflux, 12 h	 (87)	260
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h	 (98)	47

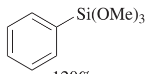
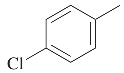
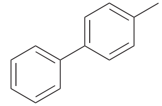
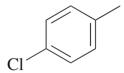
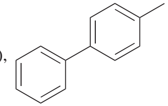
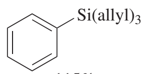
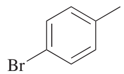
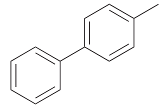
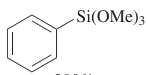
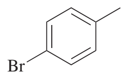
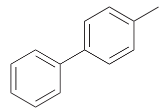
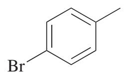
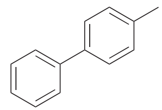
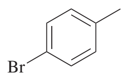
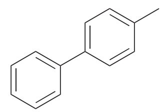
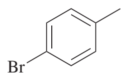
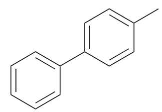
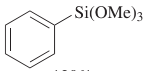
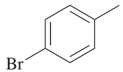
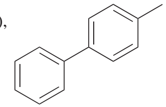
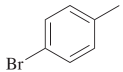
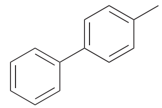
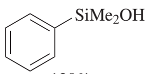
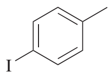
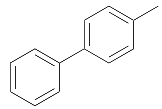
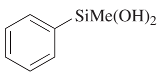
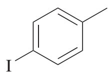
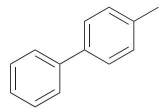
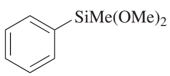
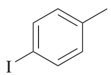
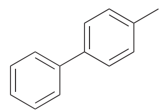
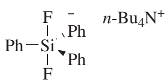
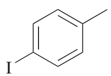
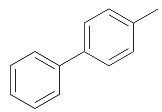
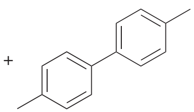
 120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•$3H_2O$ (120%), toluene, 110°, 18 h		(99)	241
200%		Pd_2dba_3 (10%), Cyclohexyl JohnPhos (15%), TBAF (200%), DMF, 87°, 27 h		(63)	236
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/ H_2O (10:1), 80°, 3 h		(96)	47
 200%		$Pd(OAc)_2$ (3%), PPh_3 (6%), TBAF (200%), DMF, 90°, 24 h		(77)	236
200%		$Pd(OAc)_2$ (10%), P(*o*-tol)$_3$ (20%), TBAF (200%), DMF, 90°, 24 h		(78)	236
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(71)	245
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(98)	237

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (94)	234
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), dioxane, 80°, 4 h	 (39)	238
 120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAT (12%), THF, 70°, 0.5 h	 (100)	201
 120%		$Pd(PPh_3)_4$ (5 %), Ag_2O (1 eq), THF, 60°, 12 h	 (81)	37
 200%		CuI (200%), $NaOC_6H_5$ (200%), DMI, 130°, 12 h	 (20)	231
 140%		$[allylPdCl]_2$ (10%), DMF, 95°, 24 h	 (86) +  (4)	69

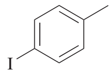
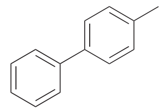
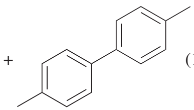
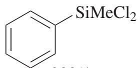
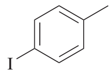
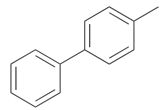
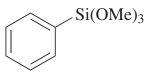
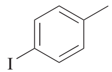
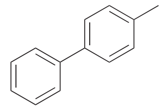
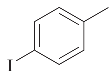
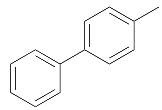
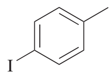
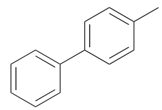
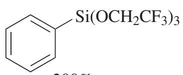
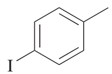
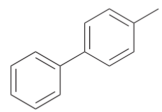
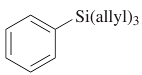
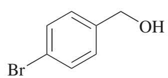
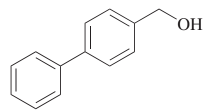
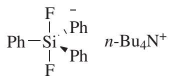
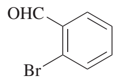
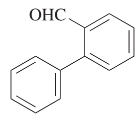
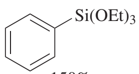
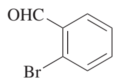
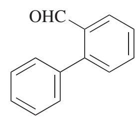
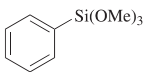
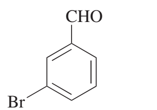
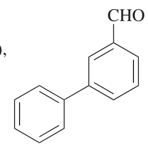
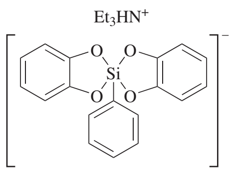
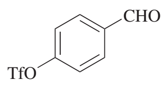
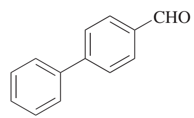
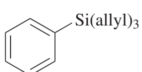
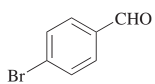
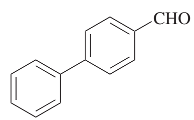
200%		Pd(dba)$_2$ (10%), THF, 95°, 25.5 h	 (64) +  (17)	69
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h	 (61)	186
 200%		Pd(dba)$_2$ (9%), TBAF (190%), DMF, 95°, 2 h	 (90)	70
220%		[allylPdCl]$_2$ (18%), TBAF (220%), DMF, 95°, 2 h	 (85)	70
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (90)	234
 200%		Pd(dba)$_2$ (9%), TBAF (200%), DMF, 95°, 2 h	 (97)	70
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h	 (79)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 6 h		(90)	270
 150%		$Pd(NH_3)_2Cl_2$ (10%), **L2** (10%), NaOH (200%), H_2O, 120°, 3 h		(88)	246
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(88)	234
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(98)	276
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (2:1), 80°, 2 h		(54)	47

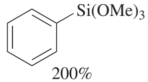
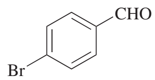
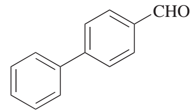
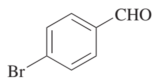
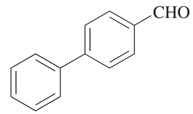
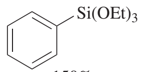
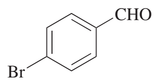
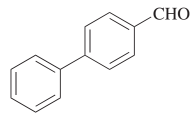
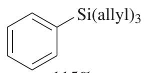
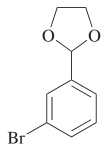
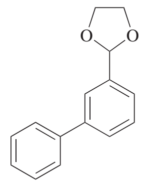
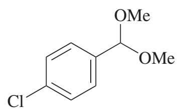
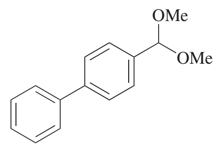
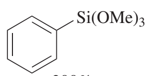
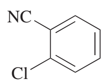
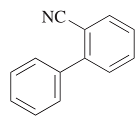
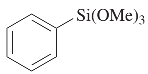
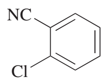
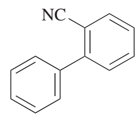
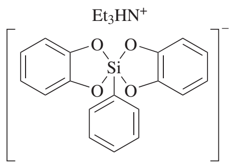
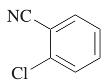
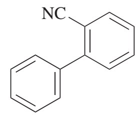
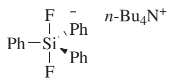
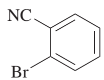
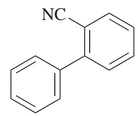
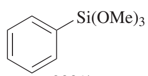
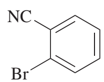
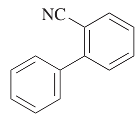
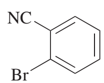
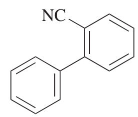
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(81)	237
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min		(88)	234
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 6 h		(60)	246
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h		(93)	47
125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(94)	47
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN, 80°, 24 h		(77)	247

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(77)	245
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(89)	276
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(54)	269
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN, 80°, 24 h		(77)	247
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(81)	245

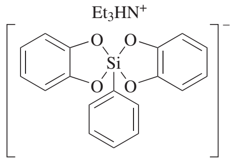
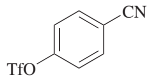
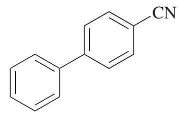
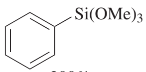
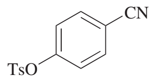
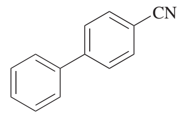
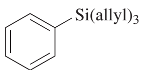
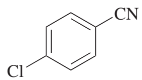
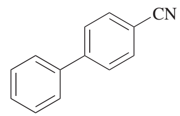
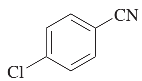
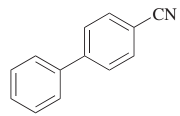
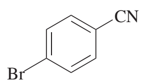
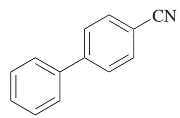
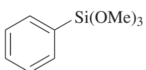
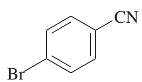
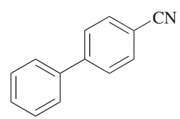
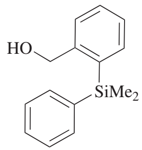
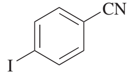
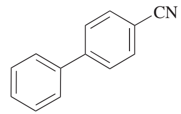
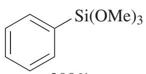
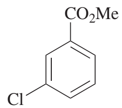
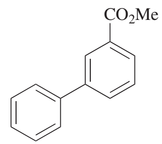
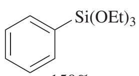
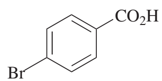
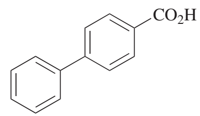
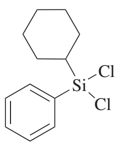
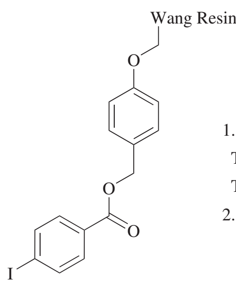
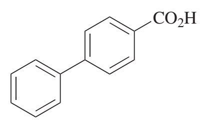
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(91)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(62)	249
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h		(77)	47
150%		TBAF•$3H_2O$ (600%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (25:1), 80°, 5 h		(74)	47
115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h		(69)	47
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(85)	237

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 7 h		(97)	151
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h		(80)	247
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 6 h		(86)	246
 1000%		1. $Pd(PPh_3)_4$ (5%), TBAF (1000%), THF, 80°, 48 h 2. TFA, CH_2Cl_2		(96)	184

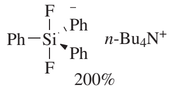
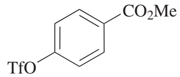
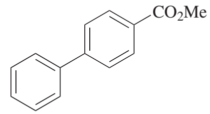
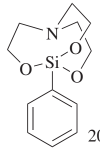
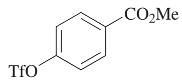
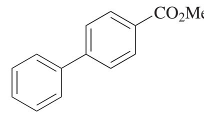
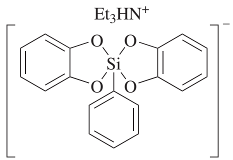
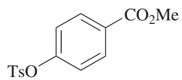
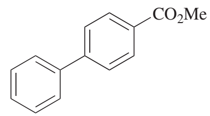
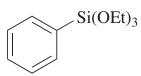
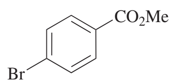
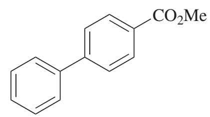
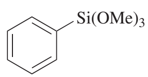
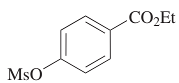
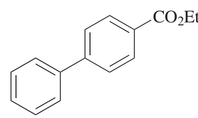
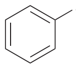
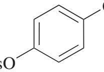
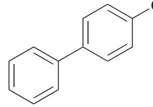
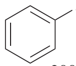
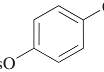
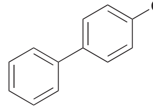
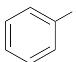
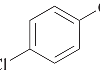
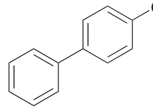
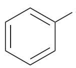
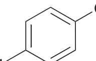
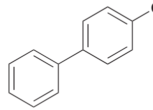
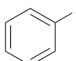
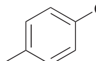
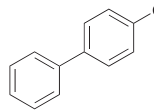
 200%		Pd(dba)$_2$ (10%), THF, 95°, 19 h		(90)	69
 200%		Pd(dba)$_2$ (10%), PPh$_3$ (20%), TBAF•3H$_2$O (200%), H$_2$O (1000%), THF, reflux, 2 h		(21)	260
 150%		Pd(dba)$_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(94)	276
 150%		Pd(NH$_3$)$_2$Cl$_2$ (0.1%), **L2** (0.1%), NaOH (200%), H$_2$O, 120°, 3 h		(84)	246
 200%		Pd(OAc)$_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(65)	248

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 $Si(OEt)_3$ 200%	 MsO, CO_2Et	$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 CO_2Et (78)	248
 $Si(OMe)_3$ 200%	 TsO, CO_2Et	$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 CO_2Et (62)	249
 $Si(allyl)_3$ 125%	 Cl, CO_2Et	TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h	 CO_2Et (71)	47
 $SiPh_2(allyl)$ 105%	 Cl, CO_2Et	TBAF•$3H_2O$ (330%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (40:1), 80°, 5 h	 CO_2Et (87)	47
 $Si(allyl)_3$ 115%	 Br, CO_2Et	TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (2:1), 80°, 3 h	 CO_2Et (75)	47

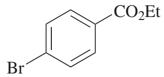
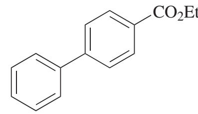
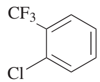
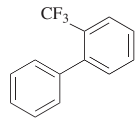
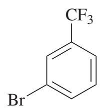
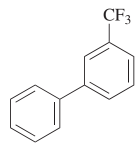
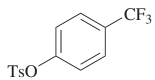
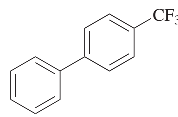
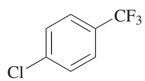
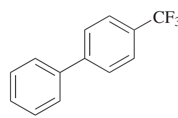
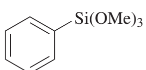
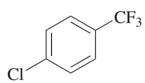
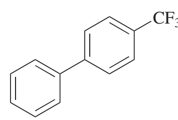
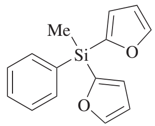
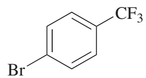
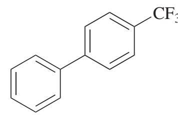
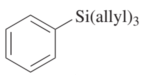
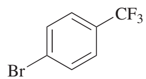
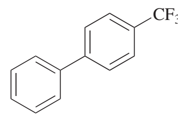
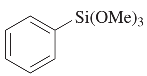
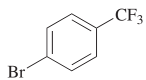
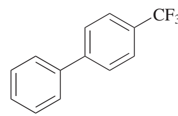
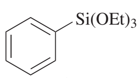
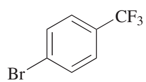
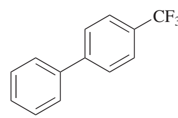
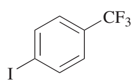
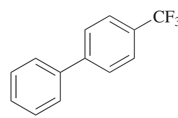
150%		TBAF•3H_2O (600%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (15:1), 80°, 11 h		(61)	47
125%		TBAF•3H_2O (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h		(86)	47
115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 2 h		(96)	47
200%		Pd(OAc)$_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(81)	249
125%		TBAF•3H_2O (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h		(95)	47
 120%		Pd(dba)$_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•3H_2O (120%), toluene, 110°, 18 h		(93)	241

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$PdCl_2$(dppf) (5%), TBAF (200%), dioxane/H_2O (8:1), 90°, 16 h	 (76)	168
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h	 (95)	47
 200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h	 (80)	237
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 3 h	 (90)	246
110%		1. TBAF (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 3 h	 (97)	46

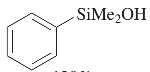
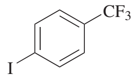
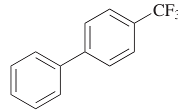
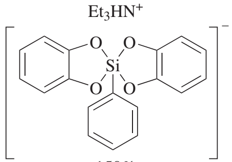
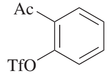
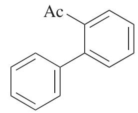
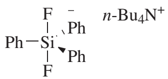
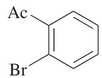
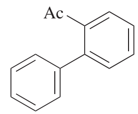
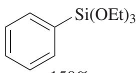
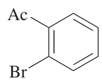
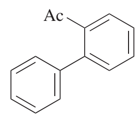
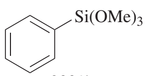
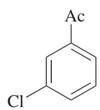
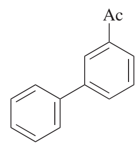
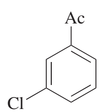
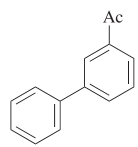
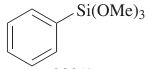
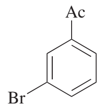
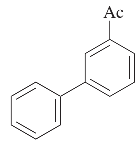
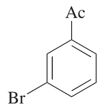
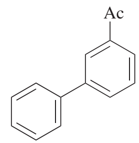
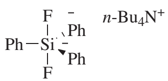
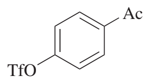
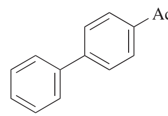
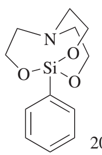
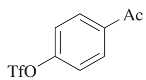
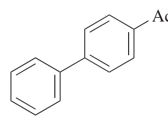
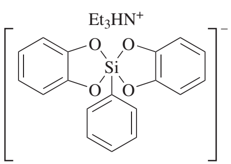
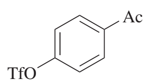
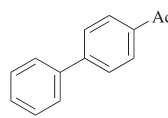
 120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAT (12%), THF, 70° 0.5 h		(86)	201
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(93)	276
 200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 6 h		(61)	270
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 48 h		(47)	246
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/ THF (5:1), 80°, 24 h		(63)	247
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(90)	245

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/ THF (5:1), 80°, 24 h	 (71)	247
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h	 (90)	245
 200%		$Pd(dba)_2$ (10%), THF, 95°, 18.5 h	 (73)	69
 200%		$Pd(dba)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), H_2O (1000%), THF, reflux, 2 h	 (56)	260
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (96)	276

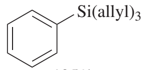
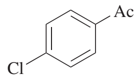
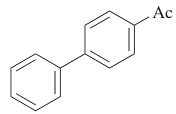
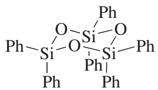
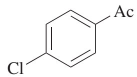
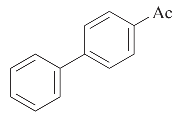
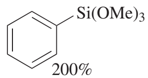
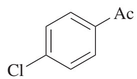
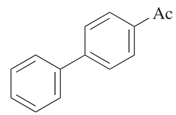
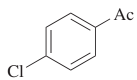
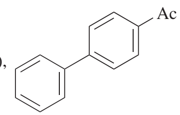
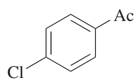
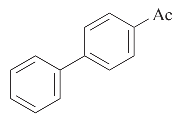
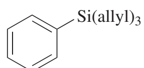
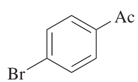
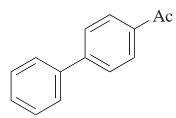
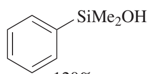
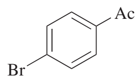
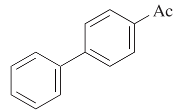
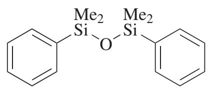
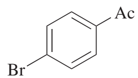
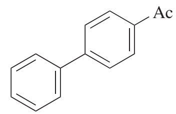
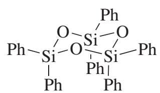
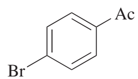
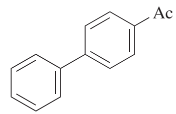
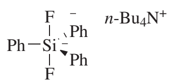
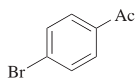
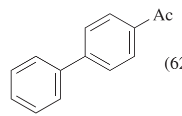
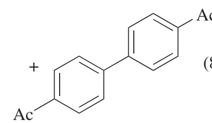
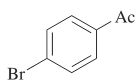
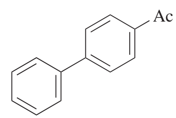
 125%		$TBAF\bullet 3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(69)	47
 20%		$Pd(OAc)_2$ (5%), KOH (880%) , dioxane/H_2O (1:1), reflux, 8 h		(15)	265
 200%		$Pd(OAc)_2$ (10%), P(*o*-tol)$_3$ (20%), TBAF (200%), DMF, 80°, 45 h		(30)	236
200%		Pd_2dba_3 (10%), Cyclohexyl JohnPhos (15%), TBAF (200%), DMF, 87°, 27 h		(47)	236
400%		$Pd(OAc)_2$ (3%), **L1** (12%), $TBAF\bullet 3H_2O$ (400%), dioxane, 80°, 24 h		(77)	238
 115%		$TBAF\bullet 3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), $DMSO/H_2O$ (10:1), 80°, 2 h		(81)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		$Pd(PPh_3)_3$ (3%), Ag_2O (100%), TBAT (12%), THF, 70°, 0.5 h	 (38)	201
 150%		$Pd(PPh_3)_3$ (5%), Ag_2O (100%), TBAT (10%), dioxane, 70°, 1 h	 (55)	201
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 0.5 h	 (97)	265
 200%		$[allylPdCl]_2$ (10%), DMF, 95°, 21 h	 (62) +  (8)	69
200%		$Pd(dba)_2$ (10%), THF, 95°, 5 h	 (90)	69

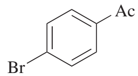
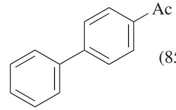
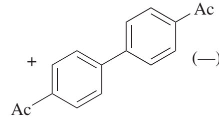
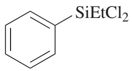
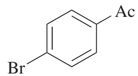
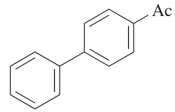
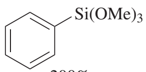
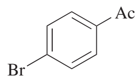
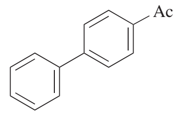
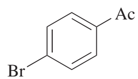
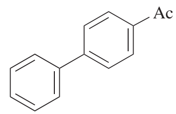
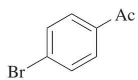
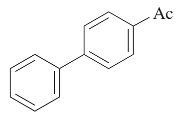
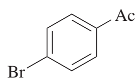
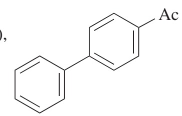
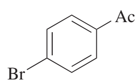
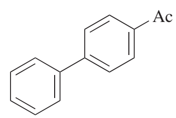
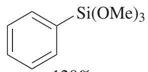
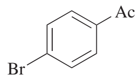
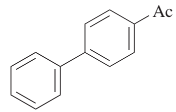
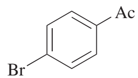
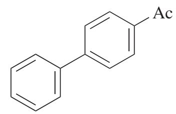
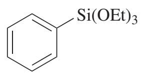
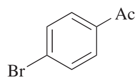
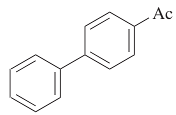
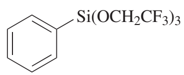
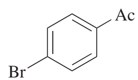
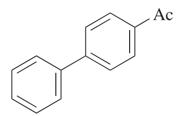
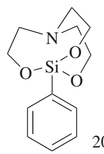
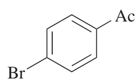
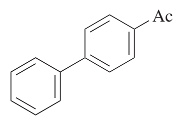
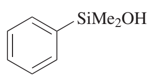
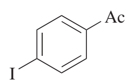
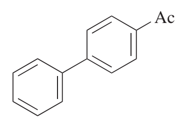
200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 4 h	 (85) +  (—)	270
 120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (1–2%), NaOH (600%), benzene, 80°, 39 h	 (89)	185
 200%		$Pd(OAc)_2$ (3%), PPh_3 (6%), TBAF (200%), DMF, 90°, 24 h	 (83)	236
200%		$Pd(OAc)_2$ (10%), $P(o\text{-tol})_3$ (20%), TBAF (200%), DMF, 90°, 24 h	 (78)	236
180%		$Pd(dba)_2$ (9%), TBAF (180%), DMF, 95°, 2 h	 (78)	70
120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 5 min	 (95)	234
180%		Pd cat. **3** (2%), NaOH (250%), H_2O, 140°, 3 h	 (80)	314

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		Pd cat. **3** (4%), TBAF (200%), *o*-xylene, 80°, 4 h	 (57)	314
200%		$Pd(OAc)_2$ (3%), **L1** (12%), TBAF•$3H_2O$ (200%), dioxane, 80°, 5 h	 (86)	238
 150%		$Pd(NH_3)_2Cl_2$ (0.01%), **L2** (0.01%), NaOH (200%), H_2O, 120°, 6 h	 (94)	246
 190%		$Pd(dba)_2$ (9%), TBAF (190%), DMF, 95°, 2 h	 (56)	70
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), THF, reflux, 2 h	 (71)	260
 120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAT (12%), THF, 70°, 0.5 h	 (98)	201

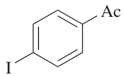
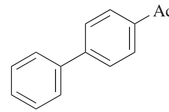
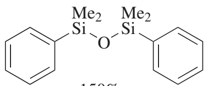
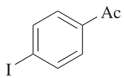
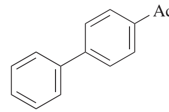
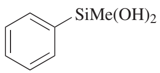
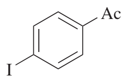
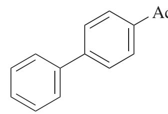
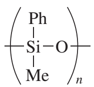
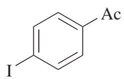
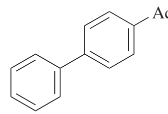
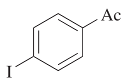
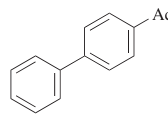
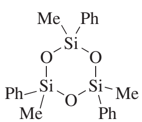
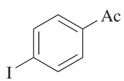
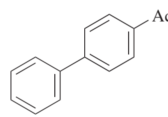
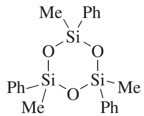
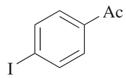
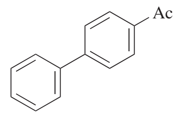
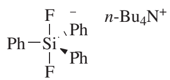
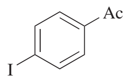
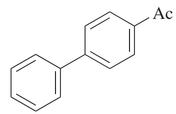
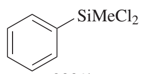
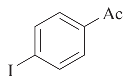
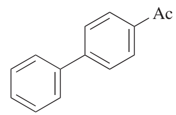
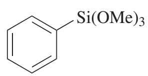
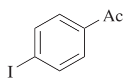
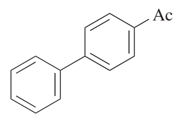
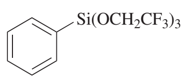
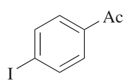
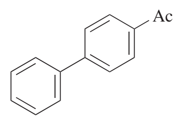
120%		$Pd(PPh_3)_4$ (3%), Ag_2O (100%), TBAF (12%), THF, 70°, 0.5 h	 (75)	201
 150%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 1 h	 (77)	201
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h	 (97)	37
 1 mmol per unit	 0.2 mmol	$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 20 h	 (67)	268
	 0.2 mmol	Pd_2dba_3•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 20 h	 (53)	268
 100%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 24 h	 (55)	268

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 100%		Pd_2dba_3•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 40 h	 (36)	268
 200%		$[allylPdCl]_2$ (10%), DMF, 95°, 21 h	 (100)	69
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h	 (81)	186
 200%		$Pd(dba)_2$ (9%), TBAF (200%), DMF, 95°, 2 h	 (58)	70
 230%		$Pd(dba)_2$ (9%), TBAF (230%), DMF, 95°, 2 h	 (78)	70

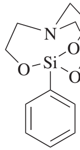
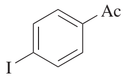
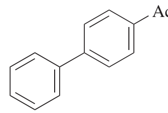
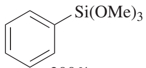
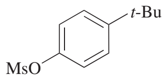
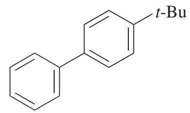
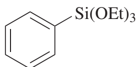
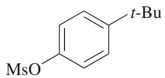
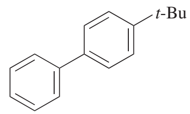
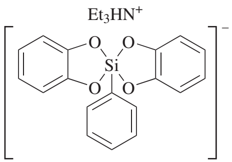
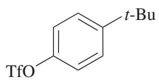
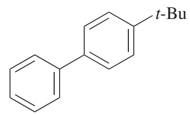
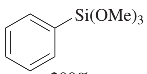
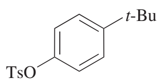
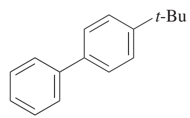
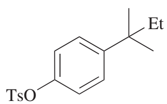
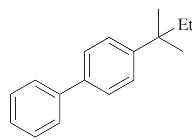
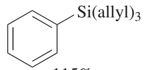
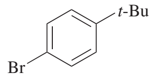
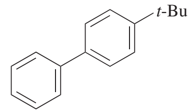
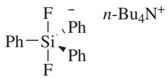
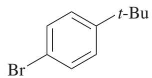
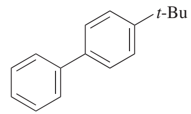
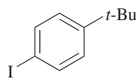
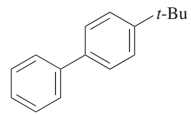
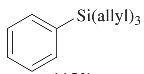
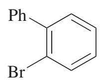
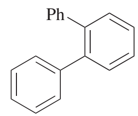
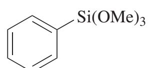
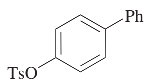
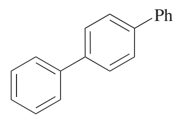
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), THF, reflux, 2 h		(80)	313
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(92)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH, 90°		(96)	248
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(95)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(88)	249
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(81)	249

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h	 (97)	47
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (66)	269
200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (87)	269
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h	 (98)	46
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (67)	249

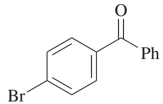
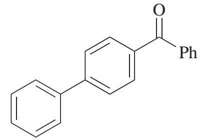
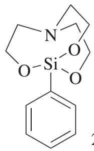
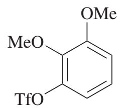
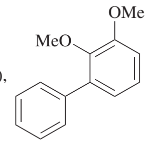
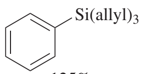
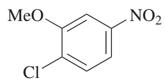
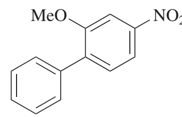
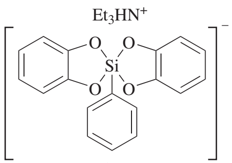
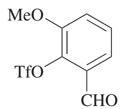
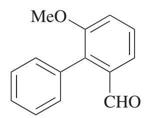
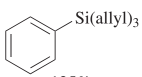
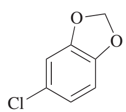
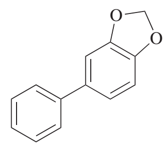
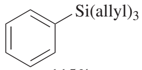
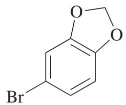
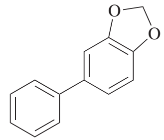
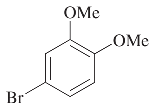
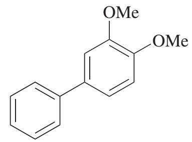
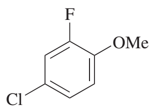
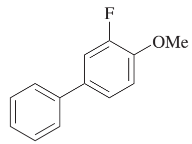
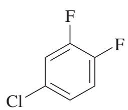
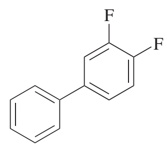
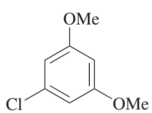
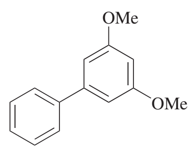
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(93)	237
 200%		$Pd(dba)_2$ (10%), Cyclohexyl JohnPhos (20%), TBAF•$3H_2O$ (200%), H_2O (2000%), THF, reflux, 12 h		(73)	260
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h		(84)	47
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h		(86)	276
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h		(97)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 2 h	 (96)	47
115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 2 h	 (97)	47
125%		TBAF•3H_2O (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h	 (95)	47
125%		TBAF•3H_2O (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h	 (89)	47
125%		TBAF•3H_2O (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 8 h	 (94)	47

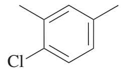
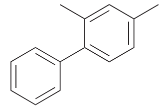
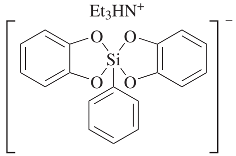
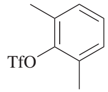
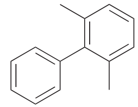
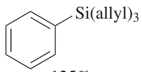
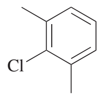
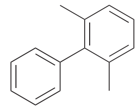
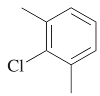
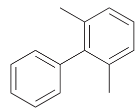
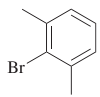
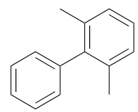
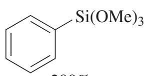
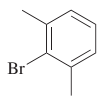
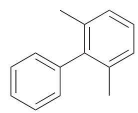
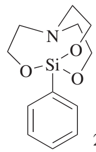
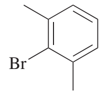
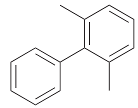
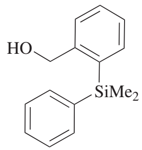
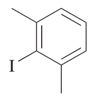
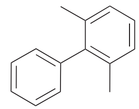
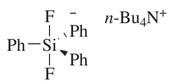
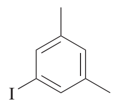
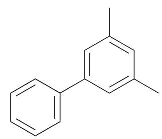
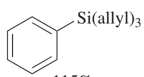
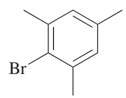
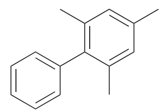
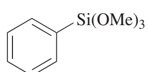
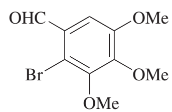
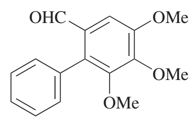
125%		TBAF•3H_2O (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(87)	47
 150%		Pd(dba)$_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h		(96)	276
 125%		TBAF•3H_2O (500%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(87)	47
150%		TBAF•3H_2O (600%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (25:1), 80°, 20 h		(57)	47
115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h		(95)	46
 200%		Pd(OAc)$_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 90°, 24 h		(85) 95% pure	236

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF•$3H_2O$ (200%), THF, reflux, 2 h		(65)	236
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 13 h		(94)	151
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(90)	315
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 6 h		(92)	47
 150%		$Pd(OAc)_2$ (5%), PPh_3 (25%), TBAF (150%), THF, reflux, 18 h		(94)	235

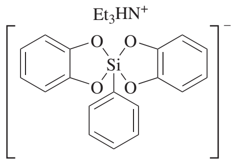
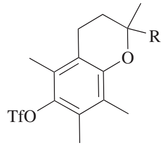
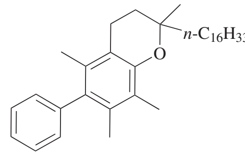
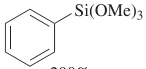
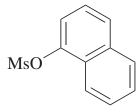
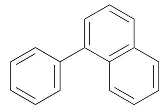
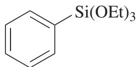
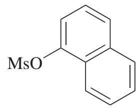
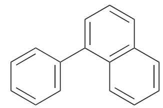
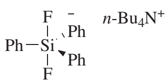
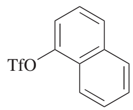
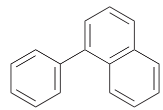
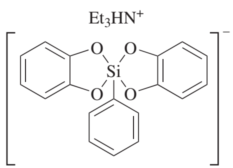
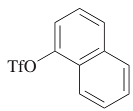
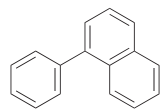
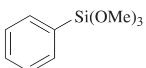
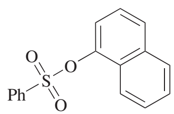
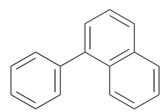
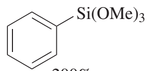
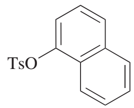
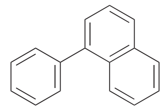
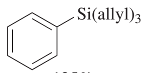
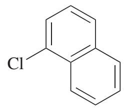
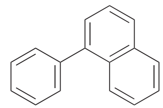
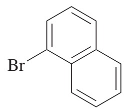
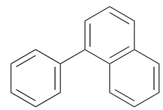
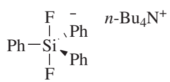
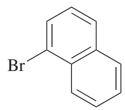
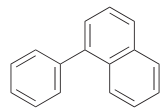
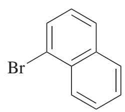
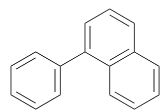
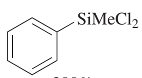
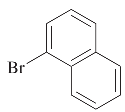
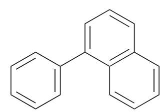
 150%	 R = n-$C_{16}H_{33}$	$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h		(90)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%) THF/t-BuOH (1:1), 90°		(81)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/t-BuOH (1:1), 90°		(71)	248
 200%		$Pd(dba)_2$ (10%), THF, 95°, 25.5 h		(71)	69
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(86)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(94)	249

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (88)	249
 125%		$TBAF•3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h	 (94)	49
115%		$TBAF•3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), $DMSO/H_2O$ (10:1), 80°, 3 h	 (96)	47
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (85)	269
200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 4 h	 (66)	270
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h	 (65)	186

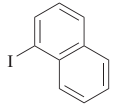
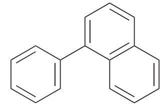
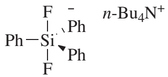
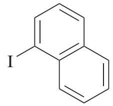
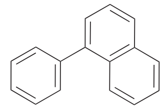
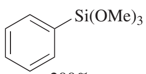
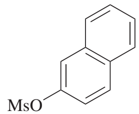
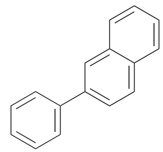
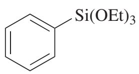
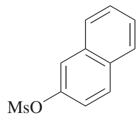
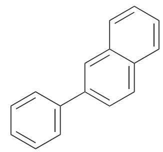
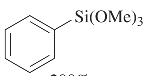
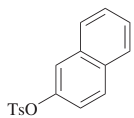
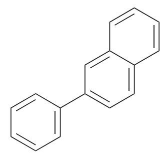
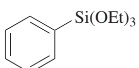
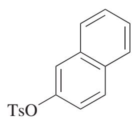
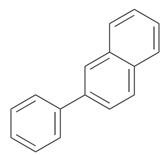
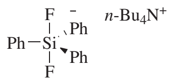
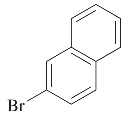
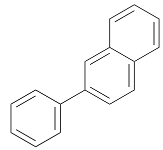
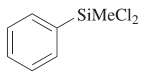
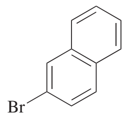
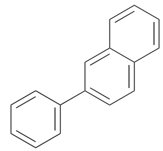
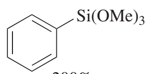
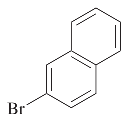
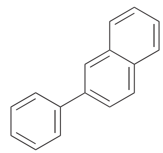
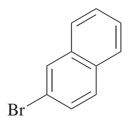
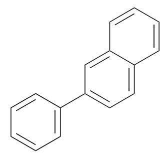
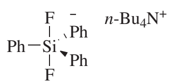
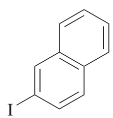
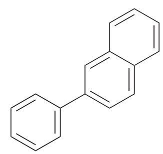
200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h		(72)	186
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(85)	269
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(83)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(84)	248
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(95)	249
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(99)	249

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(88)	269
 200%		Pd/C (5%), KOH (800%), H_2O, 100°, 12–36 h		(51)	186
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h		(81)	247
200%		Pd. cat **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(77)	245
 200%		$[allylPdCl]_2$ (2.5%), DMSO, 120°, 1 h		(83)	270

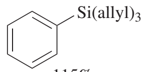
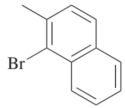
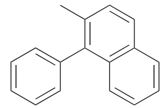
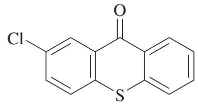
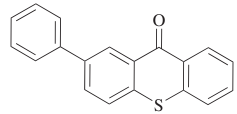
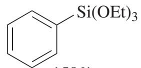
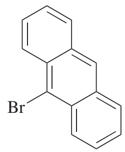
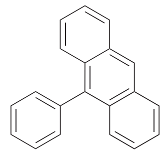
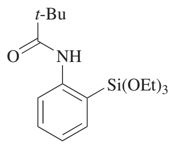
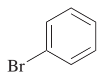
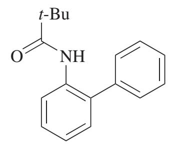
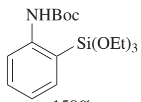
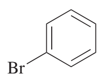
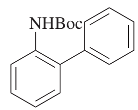
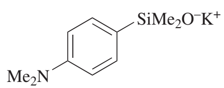
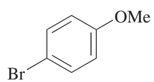
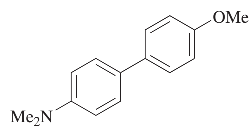
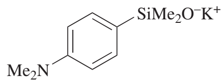
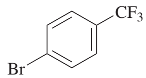
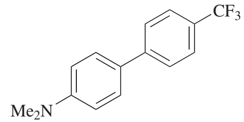
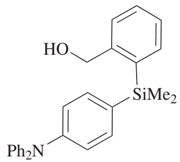
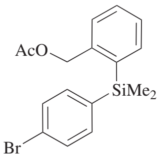
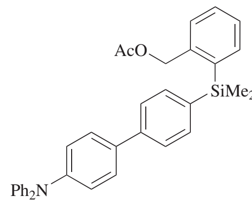
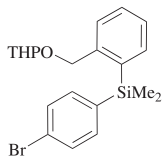
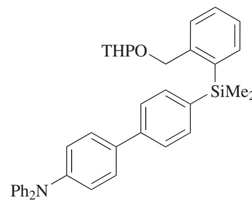
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 18 h		(99)	47
125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(98)	47
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 24 h		(88)	246
 150%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (150%), DMF, 90°, 4 h		(86)	239
 150%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (150%), DMF, 90°, 4 h		(88)	239
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(88)	54

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(73)	54
 120%		$[allylPdCl]_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 22 h		(93)	149
120%		$[allylPdCl]_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 7 h		(88)	149

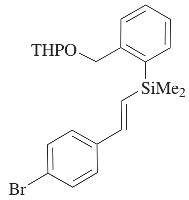
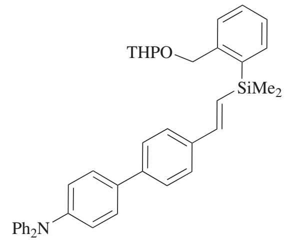
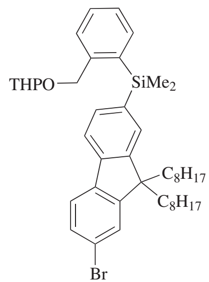
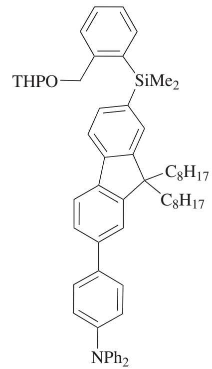
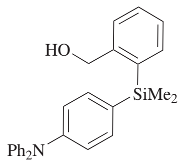
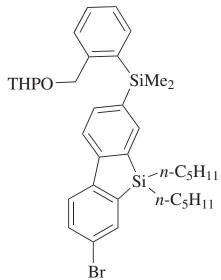
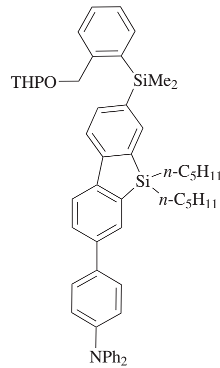
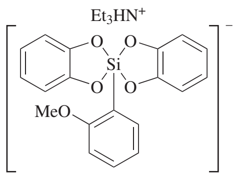
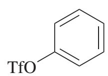
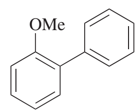
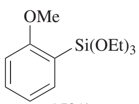
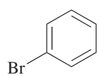
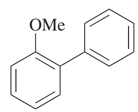
120%		[allylPdCl]$_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 17 h		(93)	149
150%		[allylPdCl]$_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 30 h		(93)	149

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$[allylPdCl]_2$ (2.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 24 h		(93)	149
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h		(41)	276
 150%		$Pd(OAc)_2$ (50%), PPh_3 (100%), TBAF (150%), DMF, 90°, 15 min		(75)	239

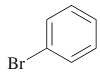
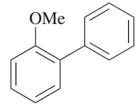
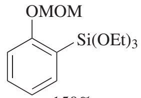
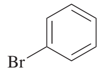
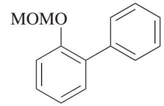
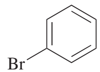
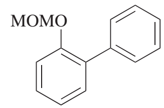
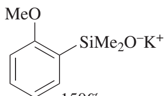
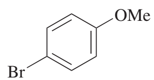
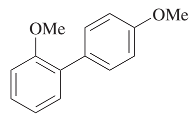
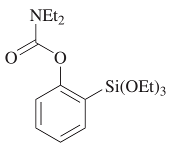
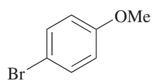
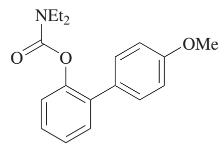
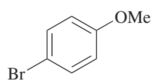
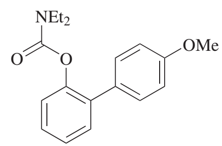
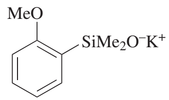
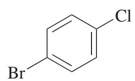
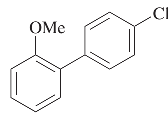
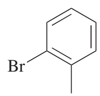
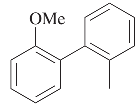
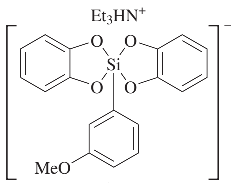
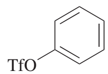
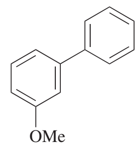
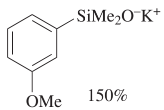
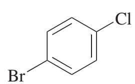
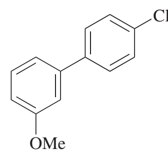
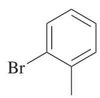
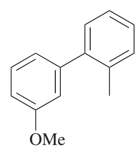
150%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (150%), DMF, 90°, 4 h		(39)	239
 150%		$Pd(OAc)_2$ (50%), PPh_3 (100%), TBAF (150%), DMF, 90°, 15 min		(87)	239
150%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (150%), DMF, 90°, 4 h		(54)	239
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 8 h		(83)	54
 150%		$Pd(OAc)_2$ (50%), PPh_3 (100%), TBAF (150%), DMF, 90°, 15 min		(49)	239
150%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (150%), DMF, 90°, 4 h		(12)	239

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 8 h	 (71)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 6 h	 (71)	54
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (87)	276
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 5.5 h	 (80)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 3 h	 (78)	54

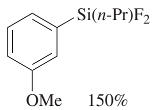
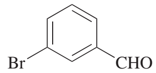
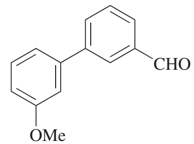
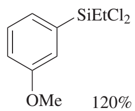
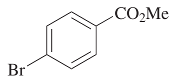
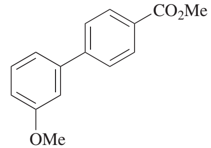
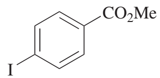
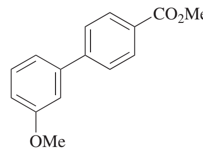
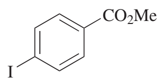
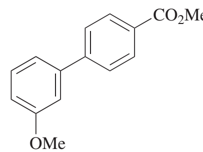
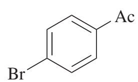
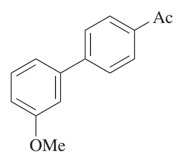
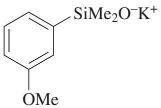
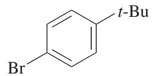
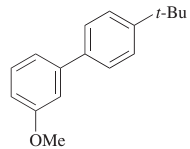
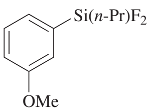
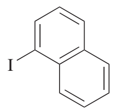
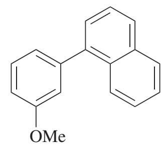
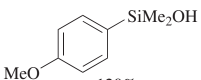
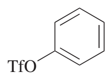
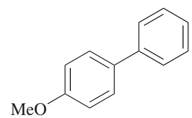
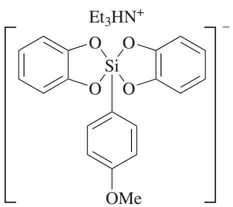
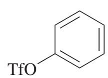
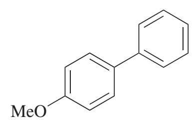
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 100°, 15 h		(83)	73
 120%		$[allylPdCl]_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(48)	73
150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 70°, 15 h		(76)	73
120%		$[allylPdCl]_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(82)	73
120%		$[allylPdCl]_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(70)	73

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 3.5 h		(82)	54
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 100°, 15 h		(94)	73
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 5 h		(1)	36
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(91)	276

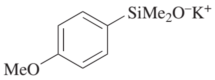
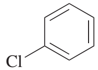
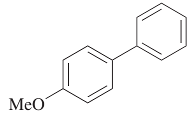
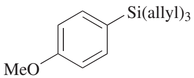
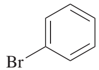
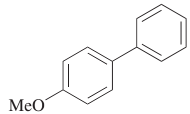
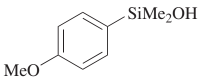
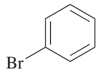
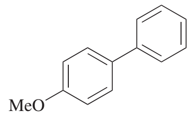
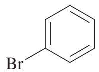
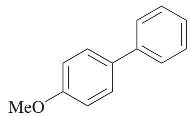
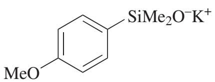
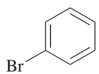
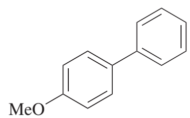
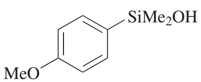
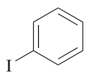
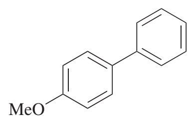
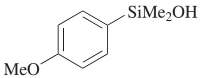
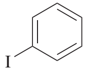
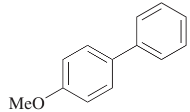
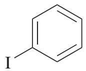
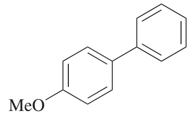
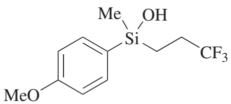
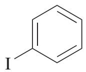
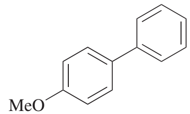
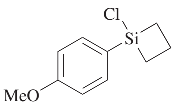
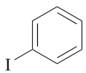
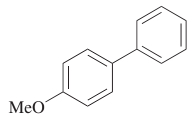
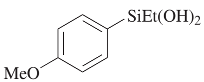
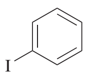
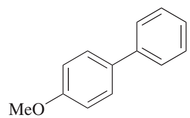
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(88)	54
 110%		1. $TBAF{\bullet}3H_2O$ (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°		(96)	46
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 5 h		(2)	36
120%		$Cs_2CO_3 + 3\ H_2O$ (200%), $[allylPdCl]_2$ (5%), dppb (10%), toluene, 90°, 12 h		(85)	204
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 30 min		(72)	218
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(80)	37

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 120%		$Pd(OAc)_2$ (5%), Ag_2O (100%), THF, 60°, 7 h		(46)	203
120%		$Cs_2CO_3 + 3\ H_2O$ (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 8 h		(91)	204
 120%		$Pd(OAc)_2$ (5%), Ag_2O (100%), THF, 60°, 7 h		(74)	203
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-}Bu)_3P$ (20%), THF, reflux, 1 h		(91)	39
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 12 h		(95)	37

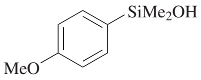
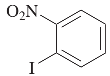
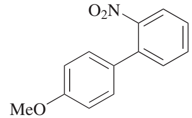
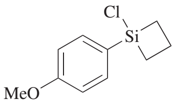
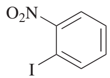
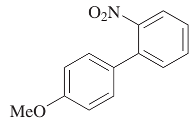
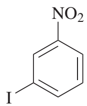
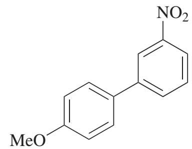
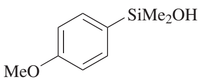
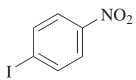
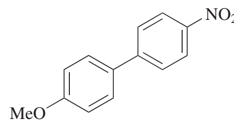
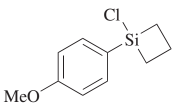
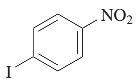
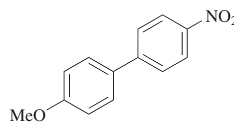
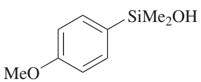
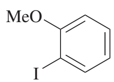
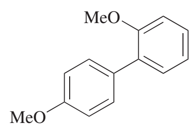
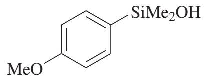
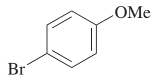
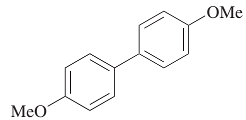
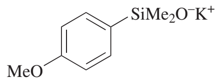
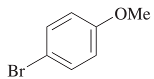
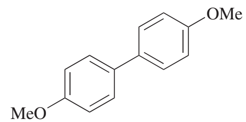
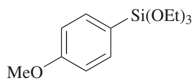
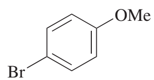
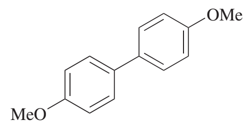
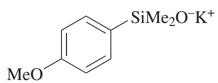
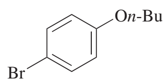
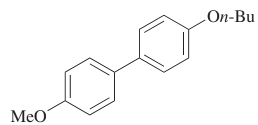
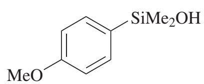
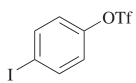
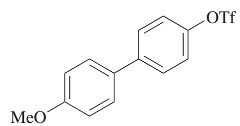
 120%		Cs_2CO_3 + 2 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), dioxane, 90°, 24 h		(83)	204, 205
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 3 h		(84)	39
120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 3 h		(90)	39
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(45)	37
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 1 h		(75)	39
 120%		Cs_2CO_3 + 2 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), dioxane, 90°, 24 h		(84)	204, 205

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), dppb (10%), toluene, 90°, 18 h	 (92)	204
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 1 h	 (81)	218
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 9 h	 (73)	246
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 1 h	 (61)	218
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h	 (55)	37

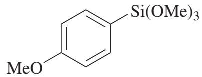
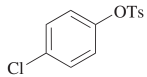
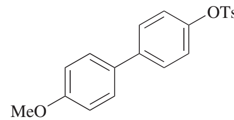
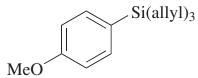
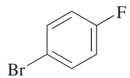
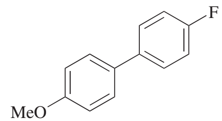
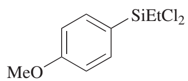
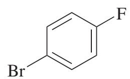
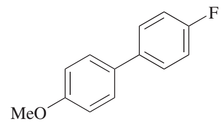
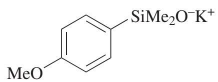
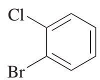
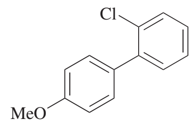
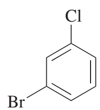
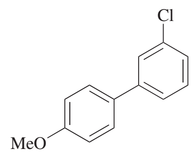
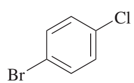
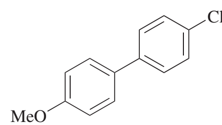
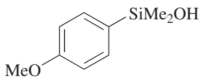
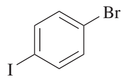
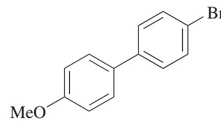
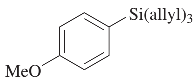
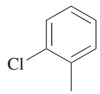
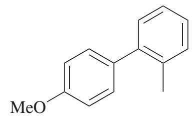
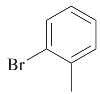
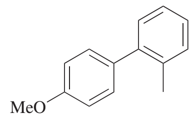
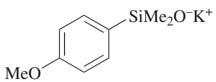
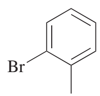
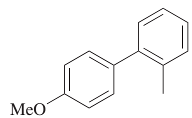
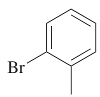
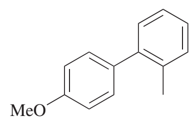
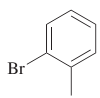
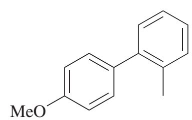
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(70)	249
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h		(98)	47
 120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(91)	73
 130%		[allylPdCl]$_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 0.5 h		(86)	218
130%		[allylPdCl]$_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 1 h		(86)	218
130%		[allylPdCl]$_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 45 min		(80)	218

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(60)	37
 120%		$TBAF•3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(93)	47
110%		1. $TBAF•3H_2O$ (440%), $DMSO/H_2O$ (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 3 h		(90)	46
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 0.5 h		(85)	218
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(88)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(88)	54

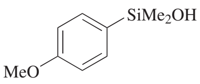
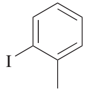
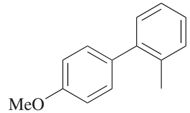
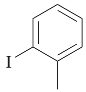
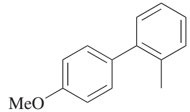
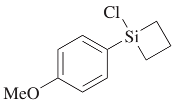
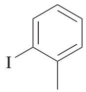
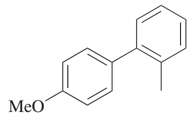
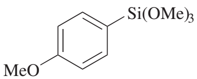
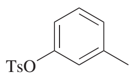
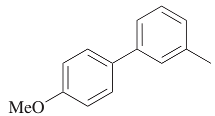
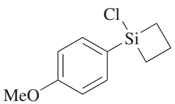
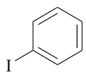
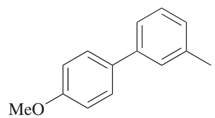
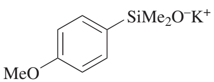
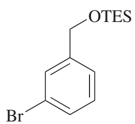
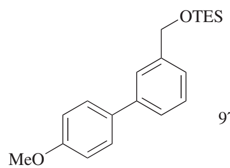
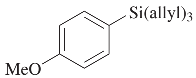
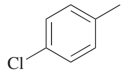
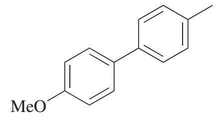
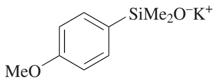
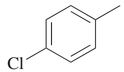
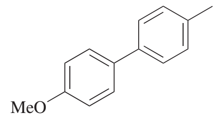
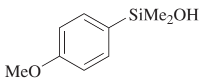
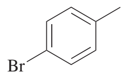
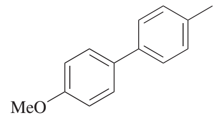
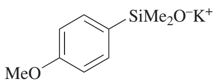
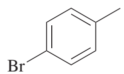
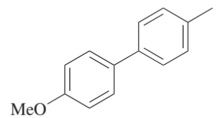
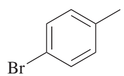
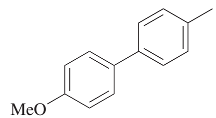
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(69)	37
120%		$Cs_2CO_3 + 2\ H_2O$ (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), dioxane, 90°, 24 h		(85)	204, 205
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-}Bu)_3P$ (20%), THF, reflux, 3 h		(89)	39
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(68)	249
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-}Bu)_3P$ (20%), THF, reflux, 1 h		(85)	39
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 1 h		(67) 97% pure by GC	218

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 120%		TBAF•$3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(95)	47
 150%		(t-$Bu_3P)_2Pd$ (5%), toluene, 90°, 7 h		(81)	54
 120%		$Cs_2CO_3 + 3\ H_2O$ (200%), $[allylPdCl]_2$ (5%), dppb (10%), toluene, 90°, 18 h		(90)	204
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 35 min		(63)	218
150%		(t-$Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(88)	54

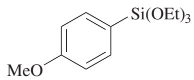
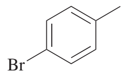
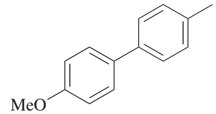
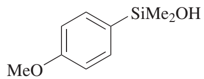
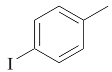
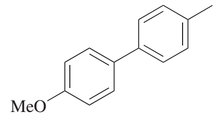
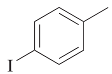
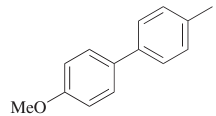
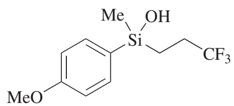
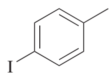
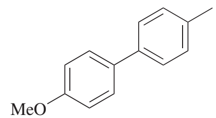
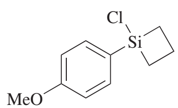
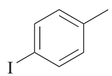
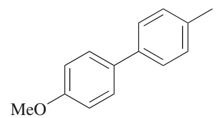
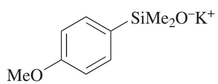
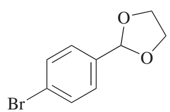
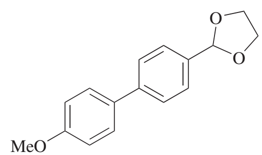
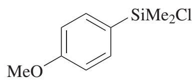
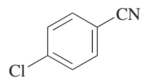
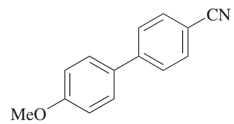
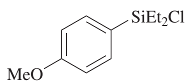
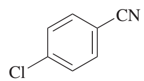
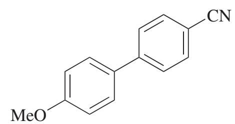
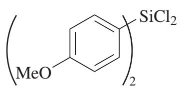
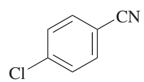
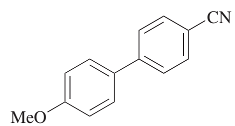
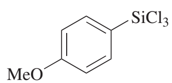
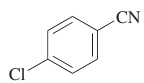
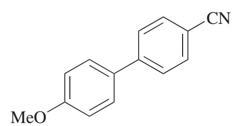
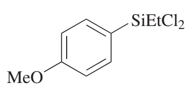
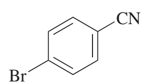
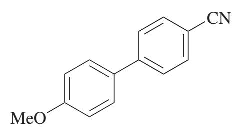
 120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), $TBAF{\bullet}3H_2O$ (120%), toluene, 80°, 18 h		(89)	241
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(75)	37
120%		$Cs_2CO_3 + 3\ H_2O$ (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 6 h		(90)	204
 120%		$Pd(OAc)_2$ (5%), Ag_2O (100%), THF, 60°, 7 h		(68)	203
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-}Bu)_3P$ (20%), THF, reflux, 1 h		(92)	39
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 4 h		(78)	54

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(93)	187
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(95)	187
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(92)	187
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(73)	187
 120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-tol})_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(67)	73

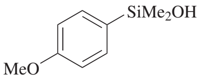
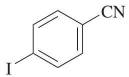
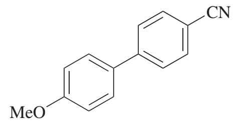
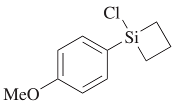
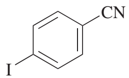
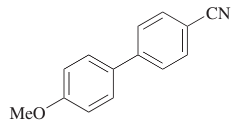
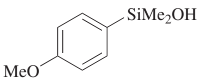
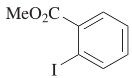
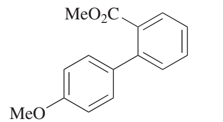
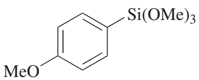
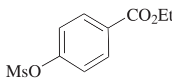
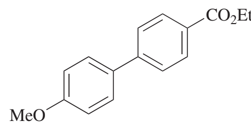
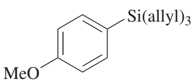
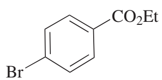
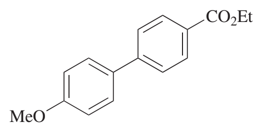
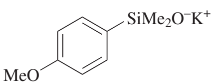
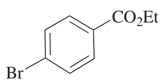
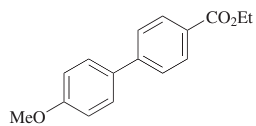
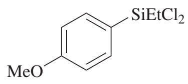
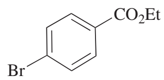
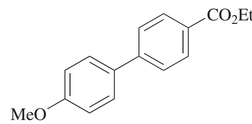
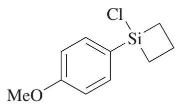
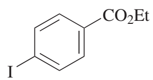
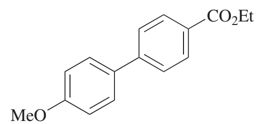
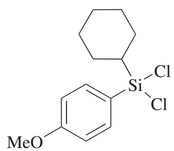
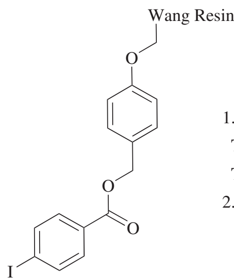
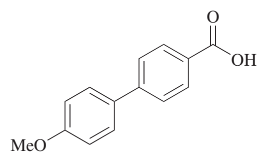
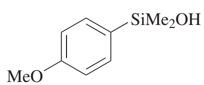
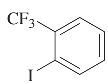
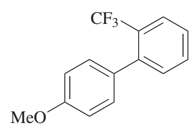
 120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 6 h		(85)	204
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 1 h		(81)	39
 120%		Cs_2CO_3 + 2 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), dioxane, 90°, 24 h		(88)	204, 205
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(50)	248
 110%		1. TBAF•$3H_2O$ (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 1 h		(72)	46
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 1 h		(82)	218

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (64)	73
 120%		TBAF (360%), [allylPdCl]$_2$ (2.5%), (*t*-Bu)$_3$P (20%), THF, reflux, 1 h	 (83)	39
 500%		1. $Pd(PPh_3)_4$ (5%), TBAF (500%), THF, 80°, 30 h 2. TFA/CH_2Cl_2 (1:3)	 (100)	184
 120%		Cs_2CO_3 + 2 H_2O (200%), [allylPdCl]$_2$ (5%), Ph_3As (10%), dioxane, 90°, 24 h	 (82)	204, 205

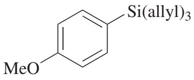
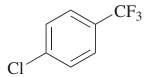
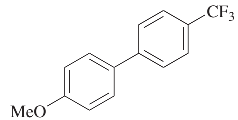
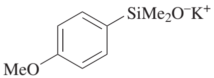
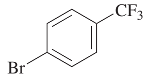
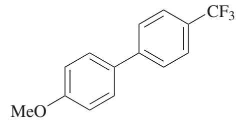
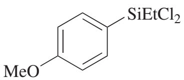
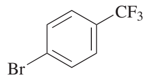
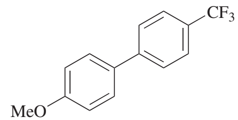
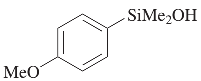
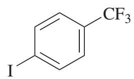
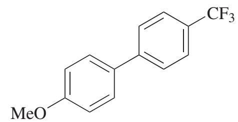
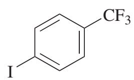
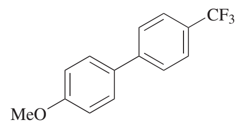
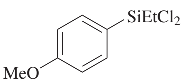
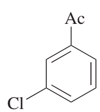
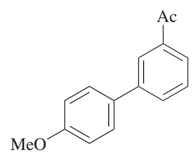
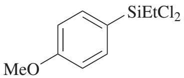
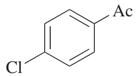
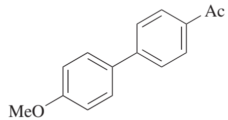
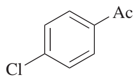
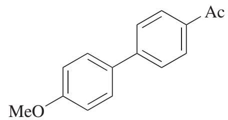
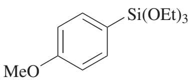
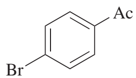
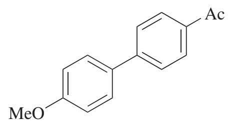
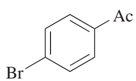
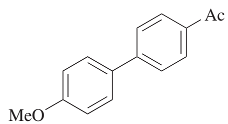
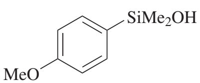
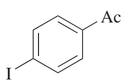
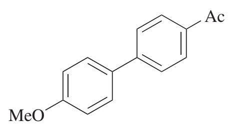
 120%		TBAF•3H_2O (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 3 h		(89)	47
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 0.5 h		(79)	218
 120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%). KF (200%), DMF, 120°, 18 h		(62)	73
 120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 3 h		(87)	204, 205
120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(54)	37
 120%		(*i*-$Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(62)	187

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h	 (62)	187
200%		$(dcpe)_2PdCl_2$ (2%), KF (1000%), DMF, 120°, 48 h	 (97)	187
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 3 h	 (70)	246
150%		$Pd(NH_3)_2Cl_2$ (0.01%), **L2** (0.01%), NaOH (200%), H_2O, 120°, 9 h	 (76)	246
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h	 (50)	37

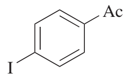
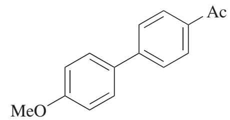
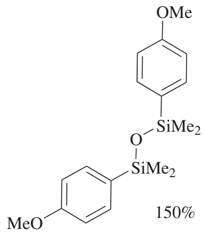
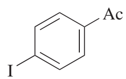
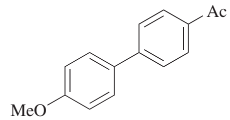
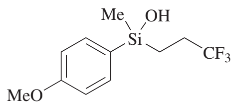
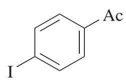
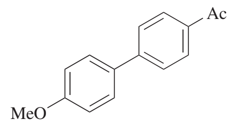
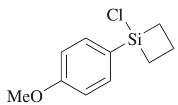
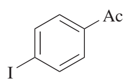
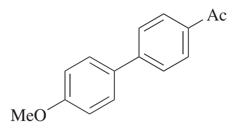
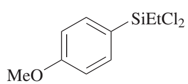
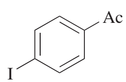
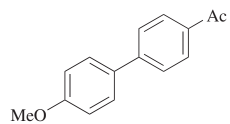
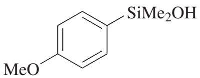
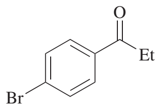
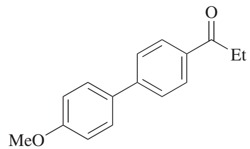
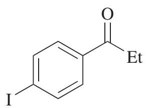
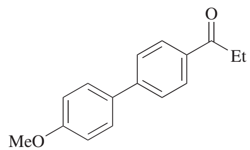
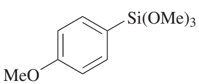
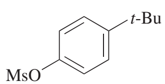
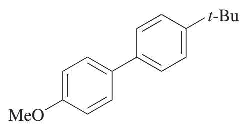
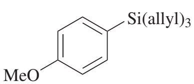
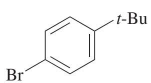
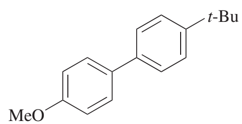
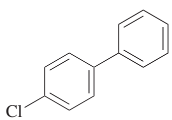
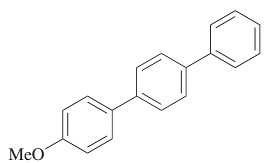
120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 3 h	 (91)	204
 150%		$Pd(PPh_3)_3$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 18 h	 (26)	201
 120%		$Pd(OAc)_2$ (5%), Ag_2O (100%), THF, 60°, 7 h	 (92)	203
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-}Bu)_3P$ (20%), THF, reflux, 1 h	 (73)	39
 120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (1–2%), NaOH (600%), benzene, 80°, 17 h	 (95)	185

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), dppb (10%), toluene, 90°, 24 h	 (90)	204
120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), Ph_3As (10%), toluene, 90°, 8 h	 (87)	204
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 (67)	248
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h	 (98)	47
120%		TBAF•$3H_2O$ (400%), $[allylPdCl]_2$ (2.5%), XPhos (10%), DMSO/H_2O (20:1), 80°, 8 h	 (87)	47

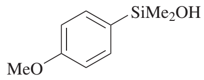
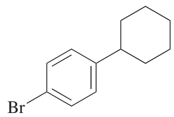
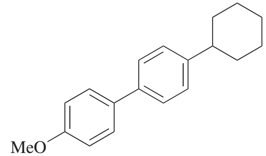
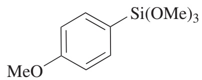
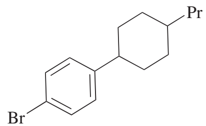
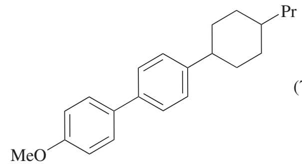
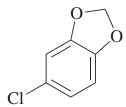
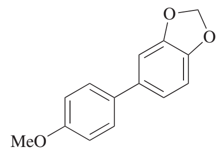
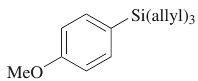
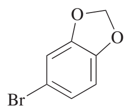
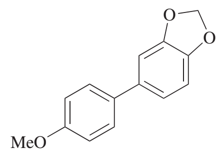
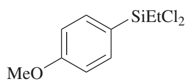
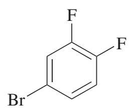
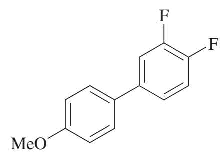
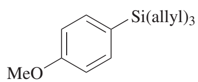
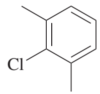
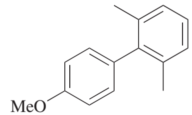
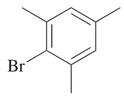
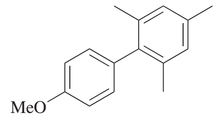
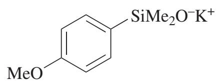
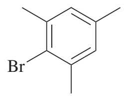
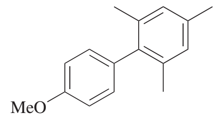
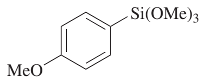
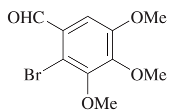
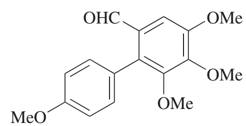
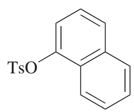
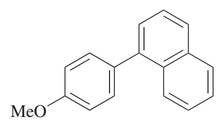
 120%		Cs_2CO_3 + 3 H_2O (200%), $[allylPdCl]_2$ (5%), dppb (10%), toluene, 90°, 18 h		(79)	204
 120%		1. TBAF (105%) 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h		(75)	187
120%		TBAF•3H_2O (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(94)	47
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 3 h		(93)	47
 120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (0.1–2%), NaOH (600%), THF, 60°, 14 h		(75)	185

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		TBAF•3H_2O (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h	 (87)	47
115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 6 h	 (97)	47
 150%		$[allylPdCl]_2$ (2.5%), dppb(O) (5%), toluene, 90°, 1 h	 (77)	218
 150%		$Pd(OAc)_2$ (5%), PPh_3 (25%), TBAF (150%), THF, reflux, 18 h	 (93)	235
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (81)	249

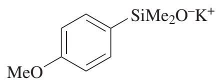
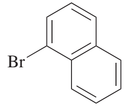
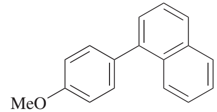
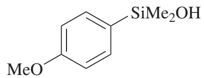
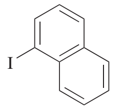
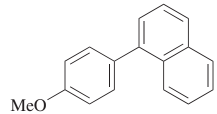
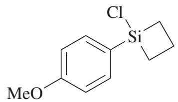
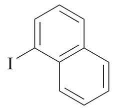
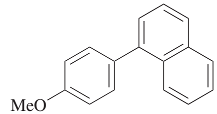
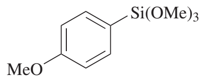
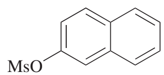
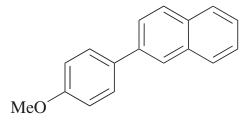
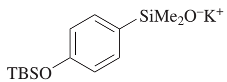
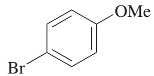
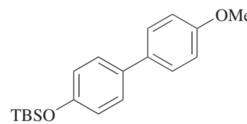
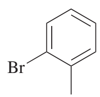
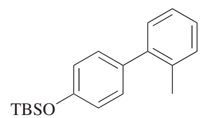
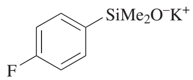
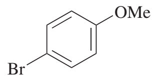
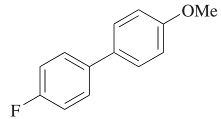
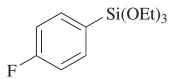
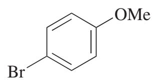
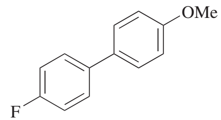
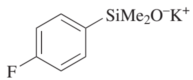
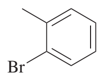
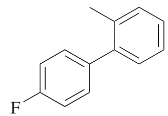
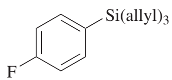
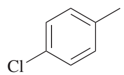
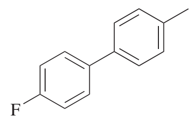
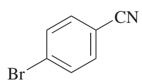
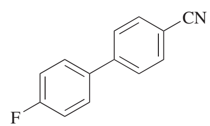
 130%		$[allylPdCl]_2$ (2.5%), $Ph_3P(O)$ (5%), toluene, 90°, 35 min	 (85)	218
 120%		$Cs_2CO_3 + 2\ H_2O$ (200%), $[allylPdCl]_2$ (5%), dppb (10%), dioxane, 90°, 24 h	 (86)	204
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 2 h	 (85)	39
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°	 (96)	248
 150%		$(t\text{-Bu}_3P)_2Pd$ (5%), toluene, 90°, 3.5 h	 (62)	54
150%		$(t\text{-Bu}_3P)_2Pd$ (5%), toluene, 90°, 3.5 h	 (34)	54

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(86)	54
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 48 h		(28)	246
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 4 h		(81)	54
 180%		TBAF•$3H_2O$ (480), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 11 h		(99)	47
180%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 18 h		(69)	47

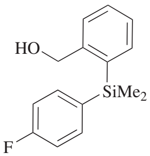
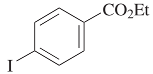
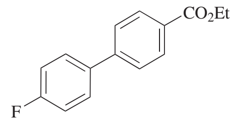
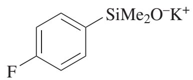
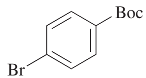
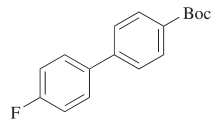
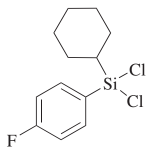
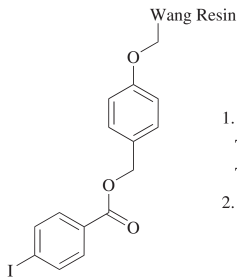
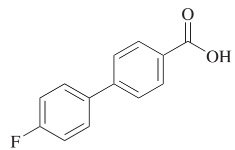
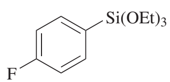
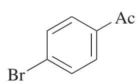
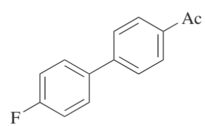
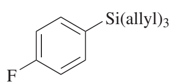
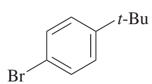
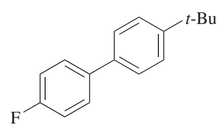
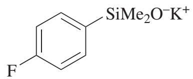
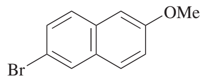
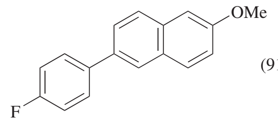
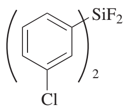
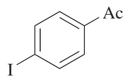
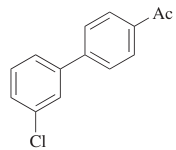
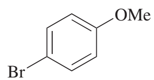
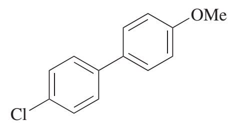
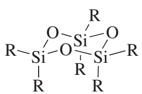
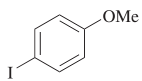
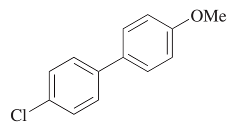
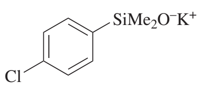
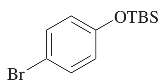
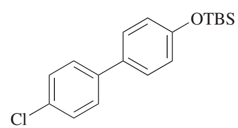
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 3 h		(91)	151
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(70)	54
 1000%		1. $Pd(PPh_3)_4$ (5%), TBAF (1000%), THF, 80°, 72 h 2. TFA, CH_2Cl_2		(91)	184
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 6 h		(68)	246
 180%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 11 h		(88)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 4 h		(91)	54
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 70°, 43 h		(74)	73
17%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 4 h		(87)	265
 R = 4-ClC_6H_4 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 4 h		(89)	265
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3.5 h		(57)	54

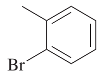
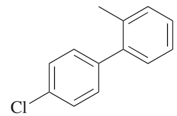
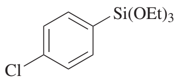
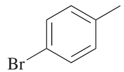
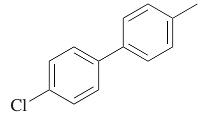
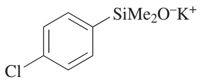
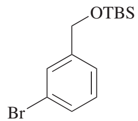
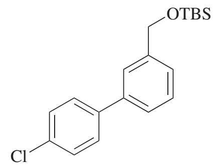
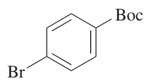
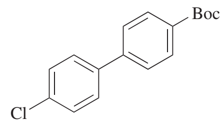
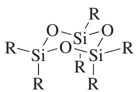
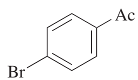
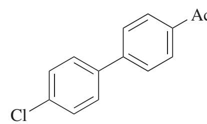
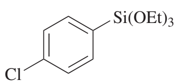
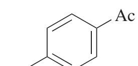
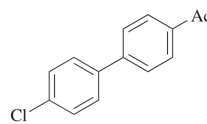
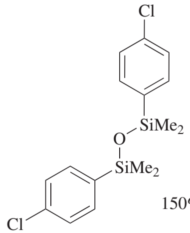
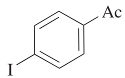
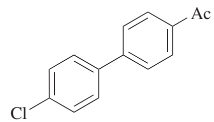
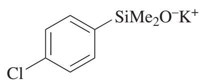
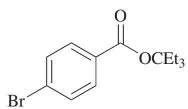
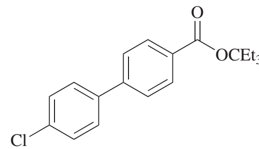
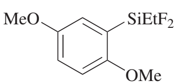
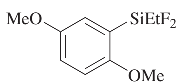
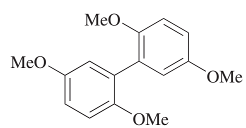
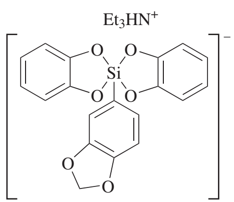
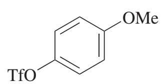
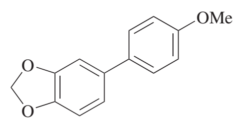
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3.5 h		(68)	54
 120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•$3H_2O$ (120%), toluene, 80°, 18 h		(78)	241
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 3.5 h		(60)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 3.5 h		(42)	54
 R = 4-ClC_6H_4 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O, reflux, 0.5 h		(88)	265
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 6 h		(72)	246

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 150%		$Pd(PPh_3)_3$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 18 h		(37)	201
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3.5 h		(56)	54
		CuCl (100%), DMF, 60°, 24 h		(77)	183
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(89)	276

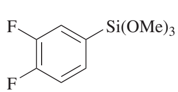
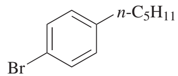
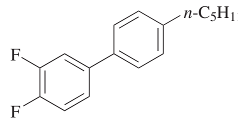
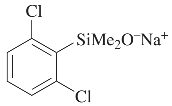
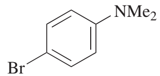
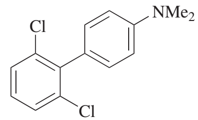
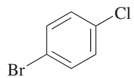
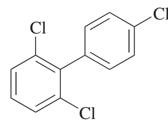
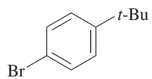
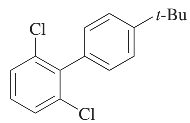
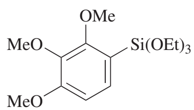
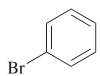
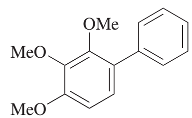
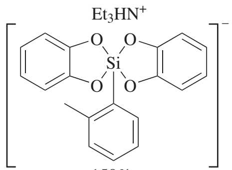
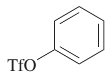
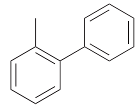
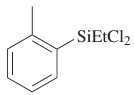
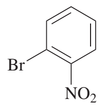
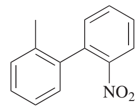
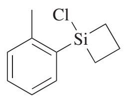
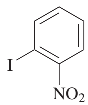
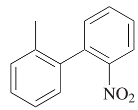
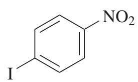
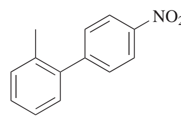
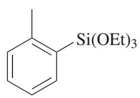
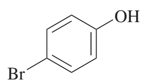
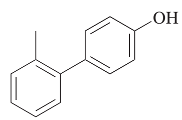
	 120%	1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h		(78)	240
 200%		$(t\text{-}Bu_3P)_2Pd$ (7.5%), THF, 90°, 3 h		(76)	54
200%		$(t\text{-}Bu_3P)_2Pd$ (7.5%), THF, 90°, 3 h		(70)	54
200%		$(t\text{-}Bu_3P)_2Pd$ (7.5%), THF, 90°, 3 h		(68)	54
 200%		$Pd(OAc)_2$ (50%), PPh_3 (100%), TBAF (150%), THF, 1 h		(70)	251

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h	 (40)	276
 120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (88)	73
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), (*t*-Bu)$_3$P (20%), THF, reflux, 3 h	 (77)	39
120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), (*t*-Bu)$_3$P (20%), THF, reflux, 2 h	 (73)	39
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 24 h	 (68)	246

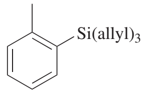
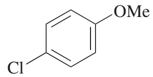
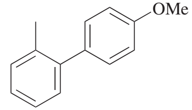
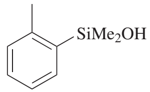
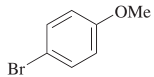
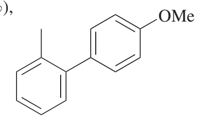
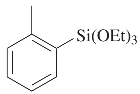
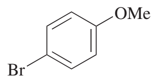
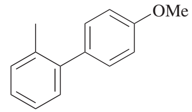
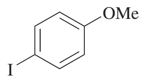
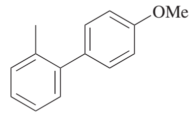
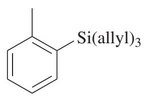
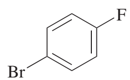
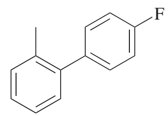
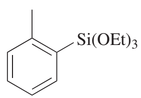
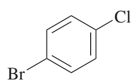
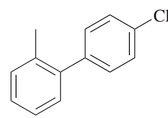
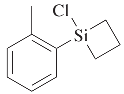
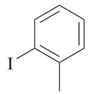
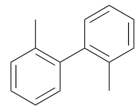
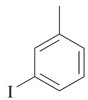
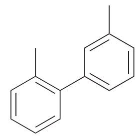
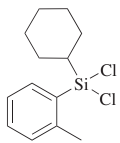
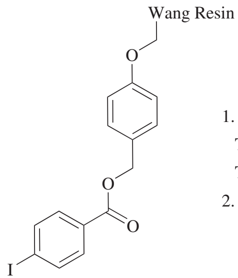
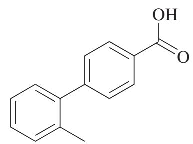
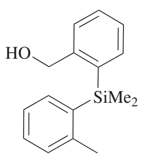
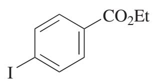
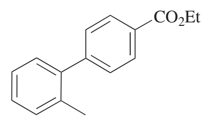
 130%		TBAF•3H_2O (480%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(92)	47
 120%		Cs_2CO_3•H_2O + 2 H_2O (200%), [allylPdCl]$_2$ (5%), dppb (10%), dioxane/toluene (4:1), 110°, 24 h		(83)	205
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 48 h		(31)	246
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(30)	37
 130%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 6 h		(79)	47
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 48 h		(44)	246

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 120%		TBAF (360%), [allylPdCl]$_2$ (2.5%), (t-Bu)$_3$P (20%), THF, reflux, 12 h		(85)	39
120%		TBAF (360%), [allylPdCl]$_2$ (2.5%), (t-Bu)$_3$P (20%), THF, reflux, 8 h		(76)	39
 1000%		1. Pd(PPh$_3$)$_4$ (5%), TBAF (1000%), THF, 80°, 48 h 2. TFA, CH_2Cl_2		(93)	184
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 80°, 5 h		(81)	151

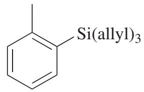
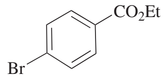
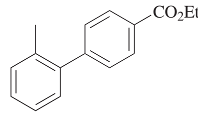
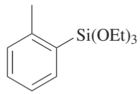
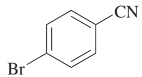
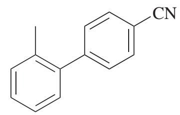
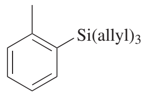
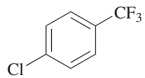
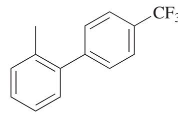
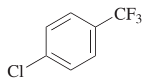
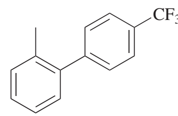
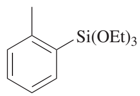
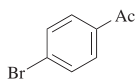
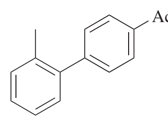
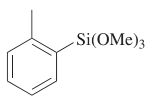
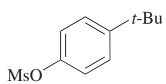
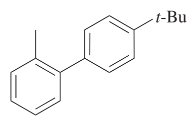
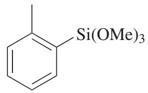
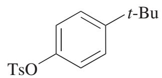
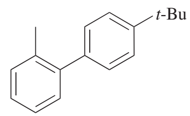
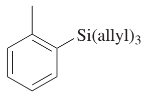
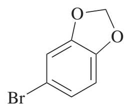
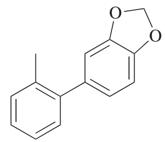
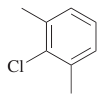
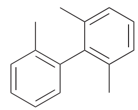
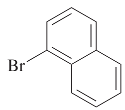
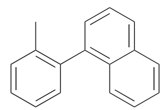
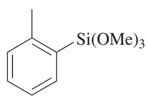
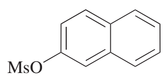
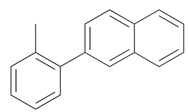
 110%		1. TBAF•3H_2O (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 1 h		(57)	46
 120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•3 H_2O (120%), toluene, 80°, 18 h		(85)	241
 130%		TBAF•3H_2O (480%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(78)	47
130%		TBAF•3H_2O (480%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(78)	160
 150%		$Pd(NH_3)_2Cl_2$ (0.01%), **L2** (0.01%), NaOH (200%), H_2O, 120°, 18 h		(89)	246
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(77)	248

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(53)	249
 130%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 8 h		(92)	47
130%		TBAF•$3H_2O$ (480%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(66)	47
130%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 20 h		(87)	47
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(85)	248

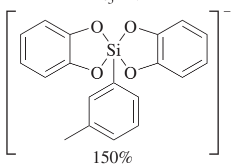
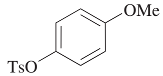
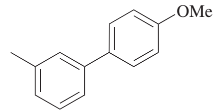
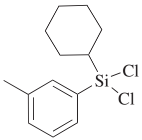
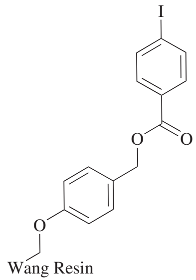
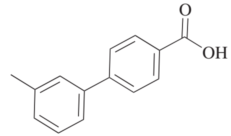
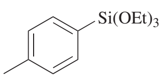
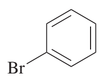
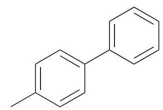
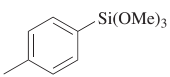
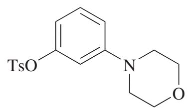
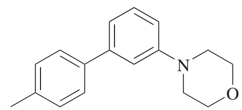
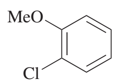
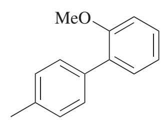
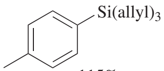
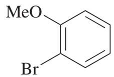
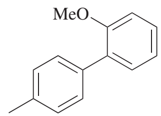
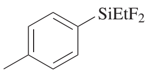
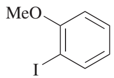
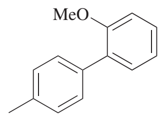
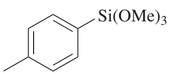
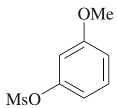
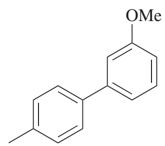
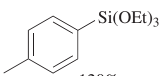
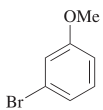
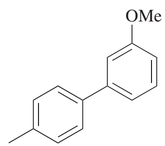
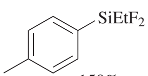
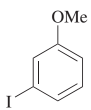
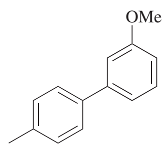
Et_3HN^+  150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(97)	125
 1000%		1. $Pd(PPh_3)_4$ (5%), TBAF (1000%), THF, 80°, 48 h 2. TFA, CH_2Cl_2		(94)	184
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 48 h		(32)	246
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(81)	249
120%		TBAF•$3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 4 h		(85)	47

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 115%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 6 h		(80)	47
 150%		$[allylPdCl]_2$ (5.0%), KF (200%), DMF, 80°, 6 h		(45)	73
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(96)	248
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 6 min		(80)	234
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 80°, 9 h		(83)	73

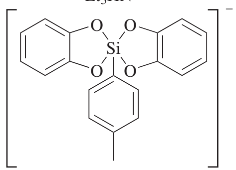
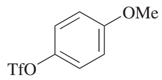
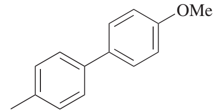
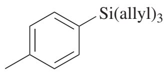
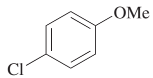
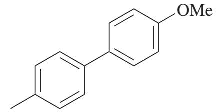
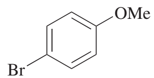
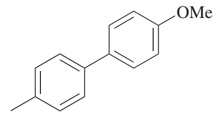
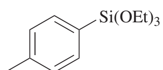
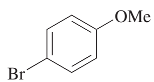
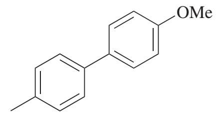
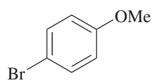
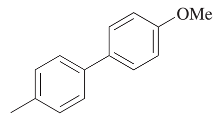
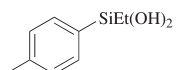
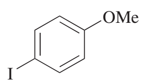
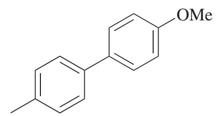
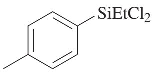
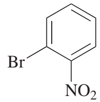
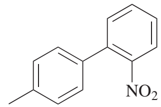
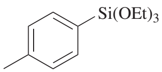
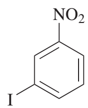
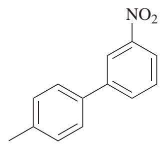
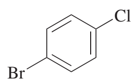
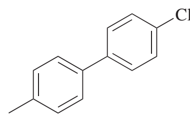
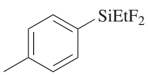
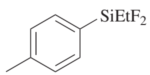
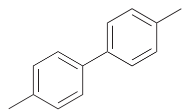
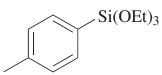
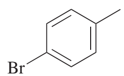
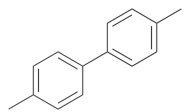
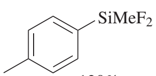
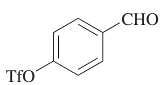
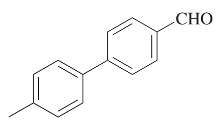
Et$_3$HN$^+$  150%		Pd(dba)$_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (92)	276
 120%		TBAF•3H$_2$O (480%), [allylPdCl]$_2$ (2.5%), XPhos (10%), THF/H$_2$O (20:1), 80°, 4 h	 (93)	47
115%		TBAF•3H$_2$O (460%), PdCl$_2$ (5%), PCy$_3$ (10%), DMSO/H$_2$O (10:1), 80°, 6 h	 (94)	47
 120%		Pd(dba)$_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•3H$_2$O (120%), toluene, 80°, 18 h	 (73)	241
150%		Pd(NH$_3$)$_2$Cl$_2$ (0.1%), **L2** (0.1%), NaOH (200%), H$_2$O, 120°, 48 h	 (37)	246
 120%		Pd(PPh$_3$)$_4$ (5%), Ag$_2$O (100%), THF, 60°, 12 h	 (99)	37

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-tol})_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(92)	73
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 6 min		(75)	234
150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 24 h		(62)	246
		CuCl (100%), DMF, 60°, 24 h		(60)	183
 120%		Na_2PdCl_4 (1.5%), SDS (20%), NaOH (600%), H_2O, 100°, 6 min		(80)	234
 120%		$Pd(PPh_3)_4$ (3–5%), TBAF (120%), THF, 50°, 4 h		(92)	181

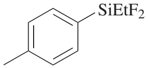
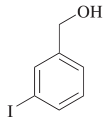
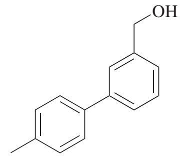
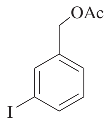
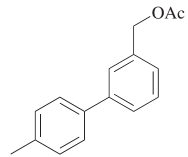
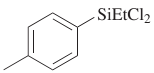
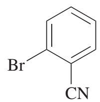
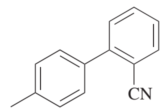
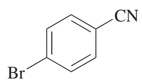
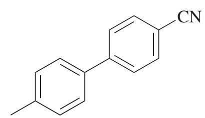
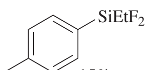
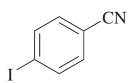
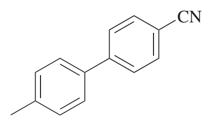
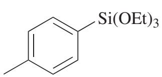
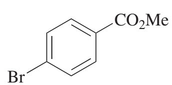
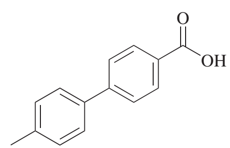
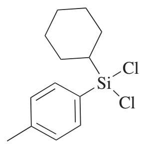
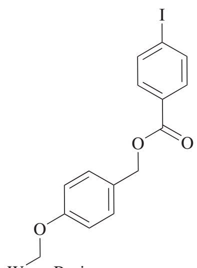
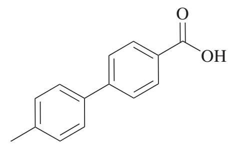
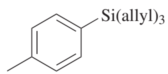
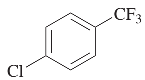
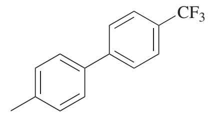
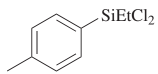
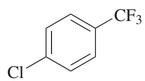
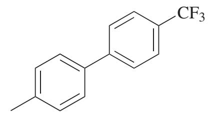
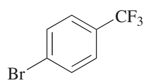
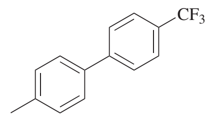
 150%		[allylPdCl]$_2$ (5%), KF (200%), DMF, 100°, 15 h		(86)	73
120–150%		[allylPdCl]$_2$ (2.5–5%), KF (200%), DMF, 100°, 49 h		(89)	180
 120%		Pd(OAc)$_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(83)	73
120%		Pd(OAc)$_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h		(70)	73
 15%		[allylPdCl]$_2$ (5%), KF (200%), DMF, 100°, 21 h		(67)	73
 150%		Pd(NH$_3$)$_2$Cl$_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 3 h		(68)	246

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 1000%	 Wang Resin	1. $Pd(PPh_3)_4$ (5%), TBAF (1000%), THF, 80°, 48 h 2. TFA, CH_2Cl_2	 (94)	184
 120%		TBAF•$3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°	 (89)	47
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h	 (68)	187
120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-}tol)_3$ (0.5%), KF (200%), DMF, 120, 18 h	 (41)	73

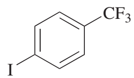
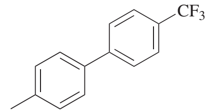
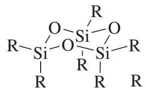
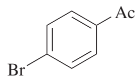
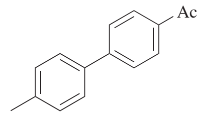
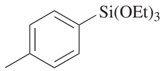
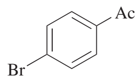
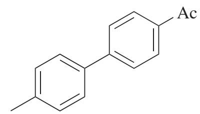
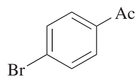
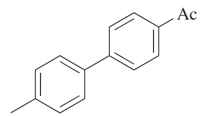
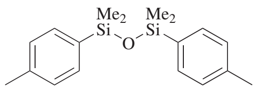
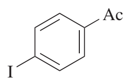
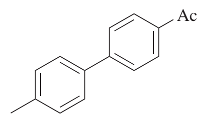
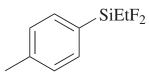
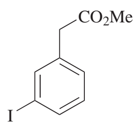
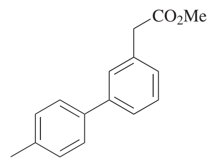
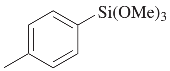
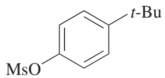
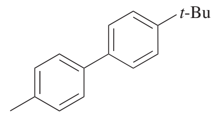
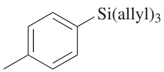
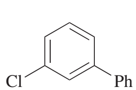
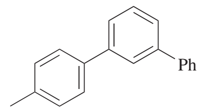
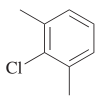
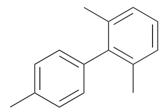
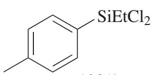
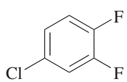
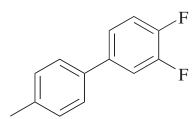
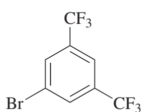
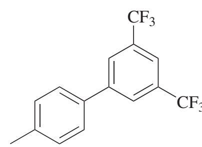
120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-tol})_3$ (0.5%), KF (200%), DMF, 120, 18 h		(91)	73
 R = *p*-tol 20%		$Pd(OAc)_2$ (5%), KOH (880%) , dioxane/H_2O (1:1), reflux, 0.5 h		(92)	265
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 3 h		(87)	246
150%		$Pd(NH_3)_2Cl_2$ (0.01%), **L2** (0.01%), NaOH (200%), H_2O, 120°, 9 h		(91)	246
 150%		$Pd(PPh_3)_3$ (5%), Ag_2O (100%), TBAT (10%), THF, 70°, 18 h		(59)	201
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 100°, 49 h		(89)	73

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(71)	248
 120%		$TBAF•3H_2O$ (400%), $[allylPdCl]_2$ (2.5%), XPhos (10%), $DMSO/H_2O$ (20:1), 80°, 8 h		(81)	47
120%		$TBAF•3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 9 h		(66)	47
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (5%), KF (600%), DMF, 120°, 24–48 h		(65)	187
120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (1–2%), NaOH (600%), THF, 60°, 39 h		(85)	185

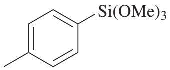
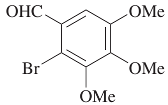
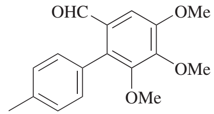
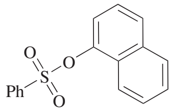
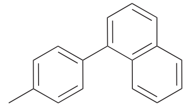
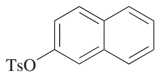
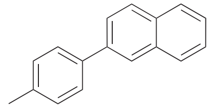
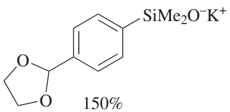
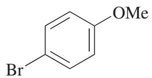
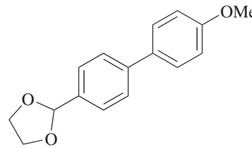
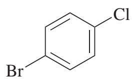
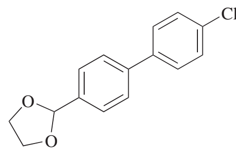
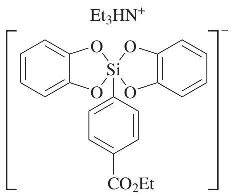
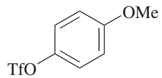
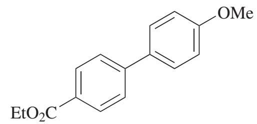
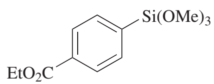
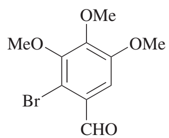
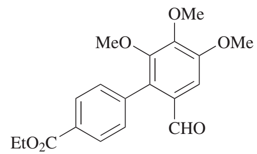
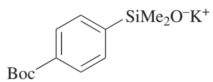
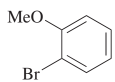
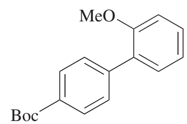
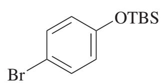
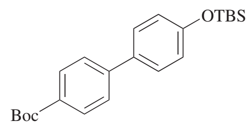
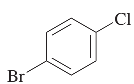
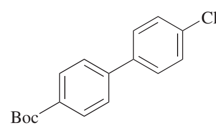
 150%		$Pd(OAc)_2$ (5%), PPh_3 (25%), TBAF (150%), THF, reflux, 18 h		(87)	235
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(63)	249
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(78)	249
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(77)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(71)	54

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (94)	276
 150%		$Pd(OAc)_2$ (5%), PPh_3 (25%), TBAF (150%), THF, reflux, 18 h	 (94)	265
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 7 h	 (69)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 6 h	 (57)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 6 h	 (79)	54

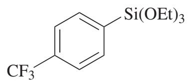
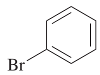
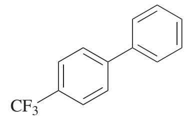
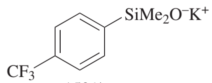
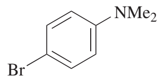
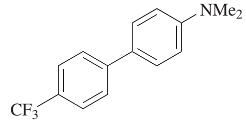
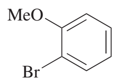
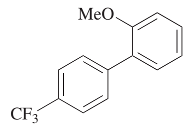
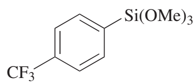
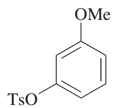
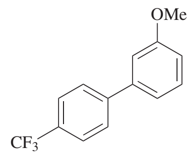
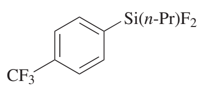
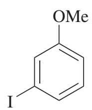
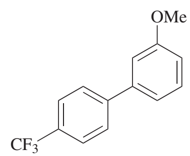
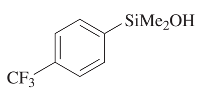
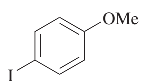
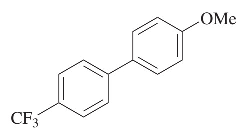
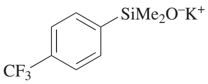
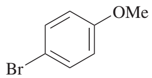
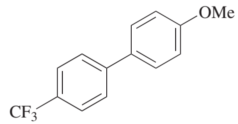
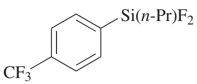
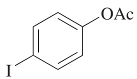
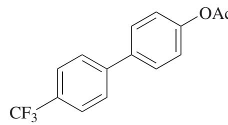
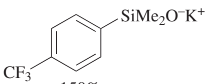
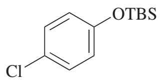
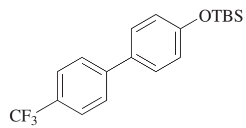
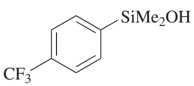
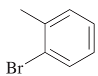
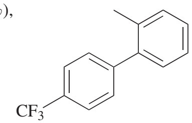
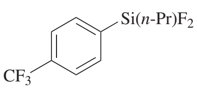
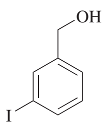
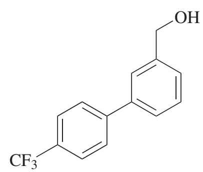
 150%		$Pd(NH_3)_2Cl_2$ (1%), **L2** (1%), NaOH (200%), H_2O, 120°, 6 h		(66)	244
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(91)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(78)	54
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(85)	249
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 80°, 28 h		(52)	73
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(84)	37

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(92)	54
 120–150%		$[allylPdCl]_2$ (2.5–5%), KF (200%), DMF, 100°, 13 h		(47)	180
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(58)	54
 120%		Cs_2CO_3•H_2O + 2 H_2O (200%), $[allylPdCl]_2$ (5%), dppb (10%), dioxane/toluene (4:1), 110°, 24 h		(26)	205
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 100°, 19 h		(64)	73

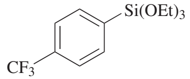
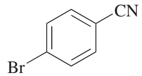
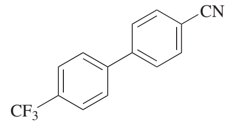
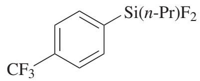
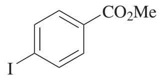
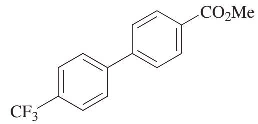
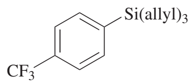
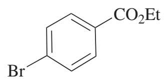
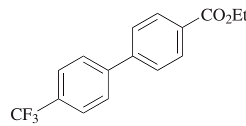
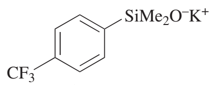
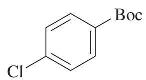
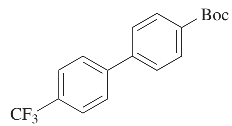
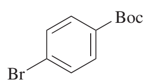
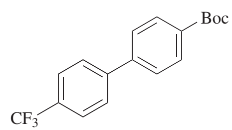
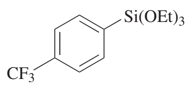
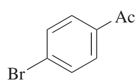
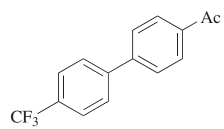
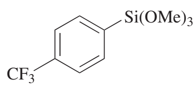
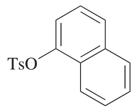
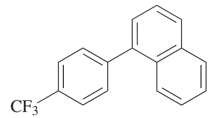
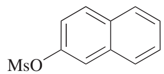
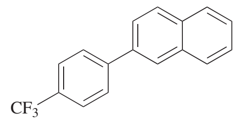
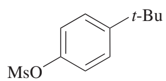
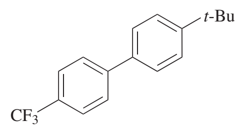
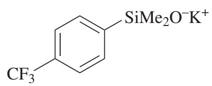
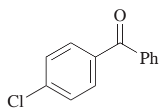
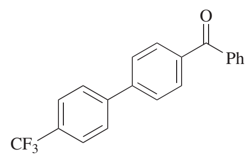
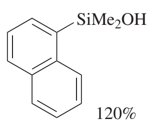
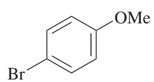
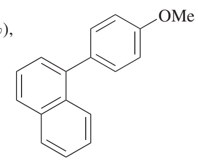
 120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), $TBAF \cdot 3H_2O$ (120%), toluene, 80°, 18 h	 (85)	241
 150%		$[allylPdCl]_2$ (5%), KF (200%), DMF, 100°, 13 h	 (47)	73
 110%		1. $TBAF \cdot H_2O$ (440%), DMSO/H_2O (10:1), rt, 1 h 2. $PdCl_2$ (5%), PCy_3 (10%), 80°, 1 h	 (49)	46
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 5 h	 (62)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h	 (68)	54
 150%		$Pd(NH_3)_2Cl_2$ (0.1%), **L2** (0.1%), NaOH (200%), H_2O, 120°, 3 h	 (76)	246

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°		(91)	249
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(90)	248
200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH (1:1), 90°		(55)	248
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(58)	54
C_{10}					
 120%		$Cs_2CO_3{\bullet}H_2O + 2\ H_2O$ (200%), $[allylPdCl]_2$ (5%), dppb (10%), dioxane/toluene (4:1), 110°, 24 h		(82)	205

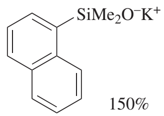
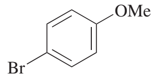
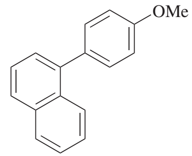
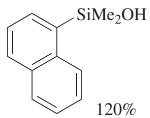
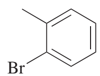
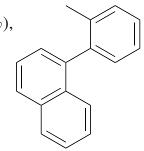
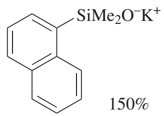
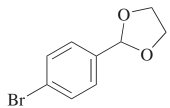
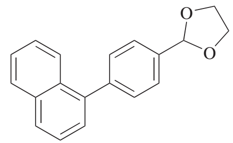
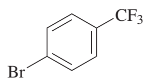
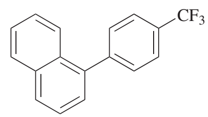
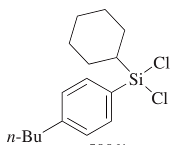
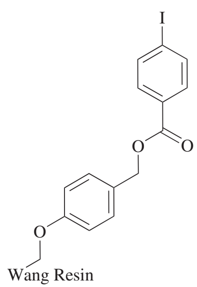
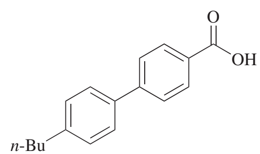
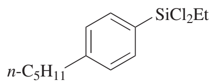
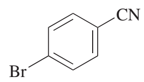
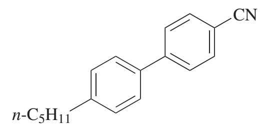
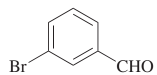
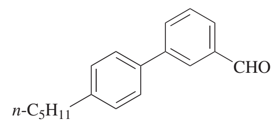
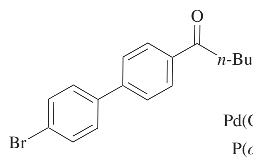
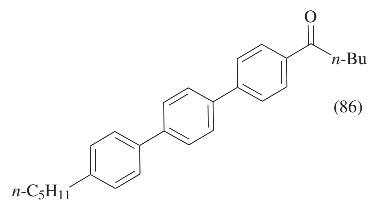
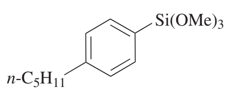
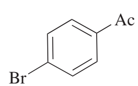
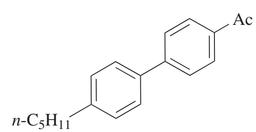
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 4 h		(82)	54
 120%		$Cs_2CO_3{\bullet}H_2O$ + 2 H_2O (200%), $[allylPdCl]_2$ (5%), dppb (10%), dioxane/toluene (4:1), 110°, 24 h		(85)	205
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 4 h		(71)	54
150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(81)	54
 500%		1. $Pd(PPh_3)_4$ (5%), TBAF (500%), THF, 80°, 30 h 2. TFA, CH_2Cl_2		(100)	184

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}				
 120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (73)	73
120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (54)	73
120%		$Pd(OAc)_2$ (0.5%), P(*o*-tol)$_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (86)	73
 120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h	 (84)	240

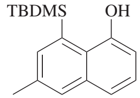
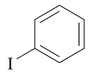
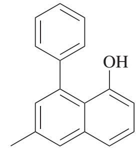
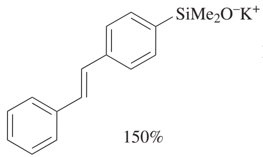
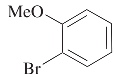
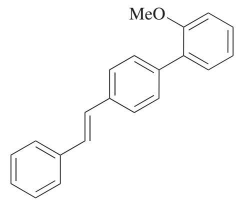
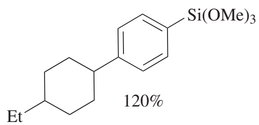
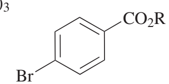
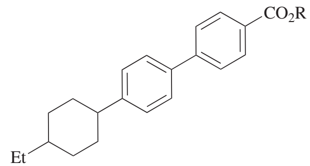
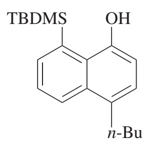
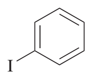
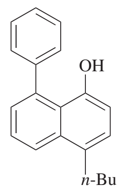
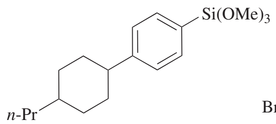
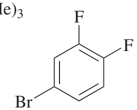
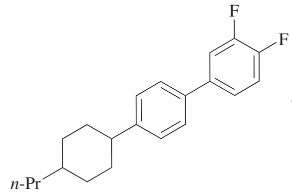
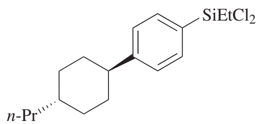
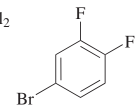
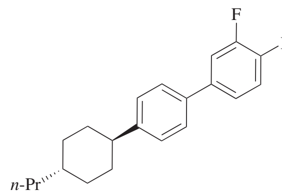
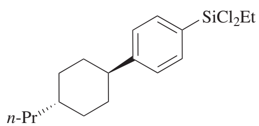
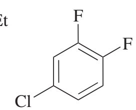
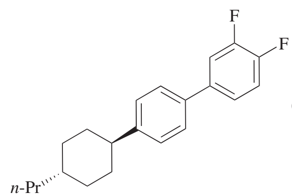
 120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 2.5 h		(72)	120
C_{14}					
 150%		$(t\text{-}Bu_3P)_2Pd$ (2.5%), toluene, 90°, 10 h		(56)	54
 120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h		R: Me (4); Et (84)	240
 120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 12 h		(61)	120

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
 120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 3 h	 (90)	240
 120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (1–2%), NaOH (600%), benzene, 80°, 62 h	 (89)	185
 120%		$Pd(OAc)_2$ (0.5%), KF (600%), DMF, 150°, 20 h	 (64)	187

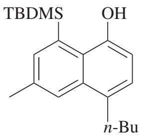
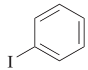
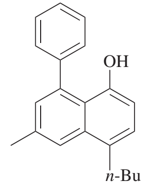
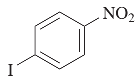
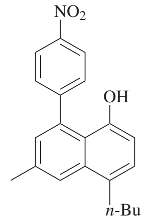
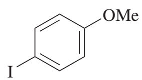
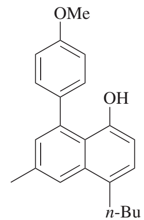
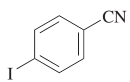
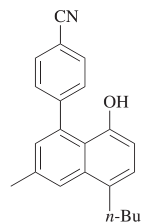
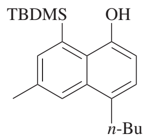
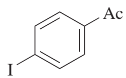
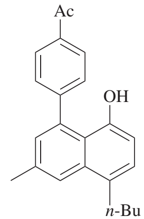
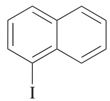
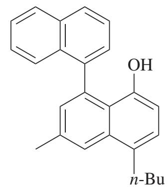
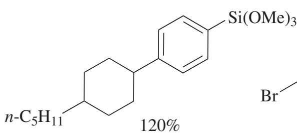
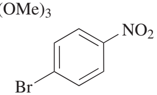
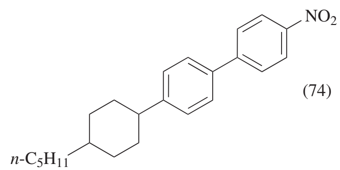
 120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 2 h		(77)	120
120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 7 h		(55)	120
120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 8 h		(80)	120
120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 2 h		(81)	120

TABLE 1A. CROSS-COUPLING OF ARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{15}					
 120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 2 h		(68)	120
120%		$[allylPdCl]_2$ (6%), $AsPh_3$ (24%), Cs_2CO_3 (150%), DME, 60°, 1.5 h		(46)	120
C_{17}					
 120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 25 h		(74)	240

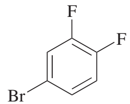
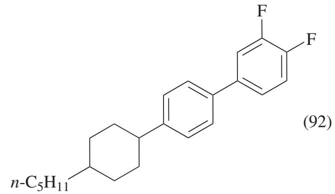
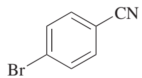
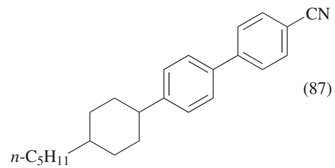
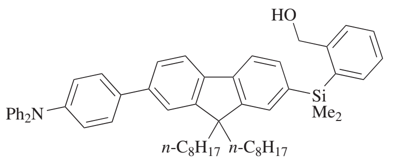
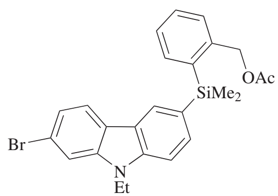
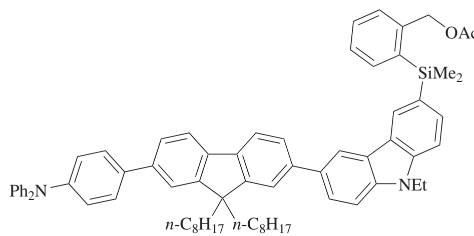
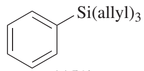
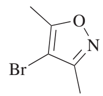
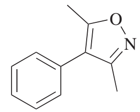
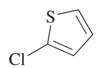
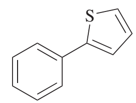
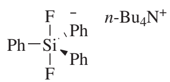
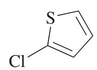
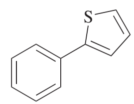
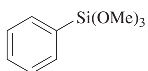
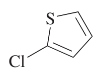
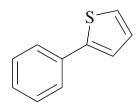
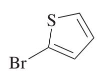
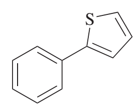
	120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 10 h	 (92)	240
	120%		1. TBAF (105%), 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h	 (87)	240
C_{35}	 100%	+ 	$[allylPdCl]_2$ (0.5%), RuPhos (2%), CuI (3%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 17 h	 (81)	149

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 18 h	 (61)	47
125%		1. TBAF (500%), THF/H_2O (20:1, 5 mL), rt, 1 h 2. $[allylPdCl]_2$ (2.5%), XPhos (10%), 80°, 12 h	 (93)	160
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (66)	269
 200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h	 (44)	245
200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 90°, 24 h	 (64)	236

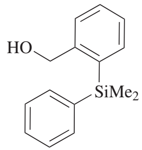
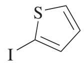
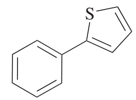
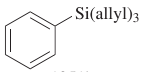
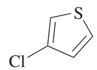
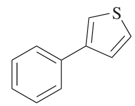
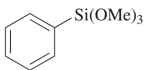
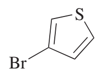
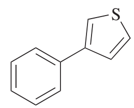
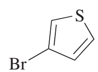
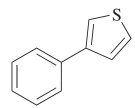
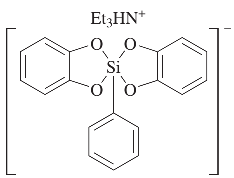
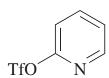
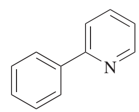
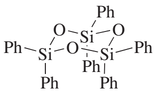
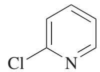
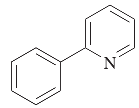
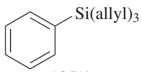
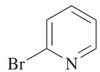
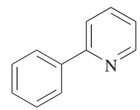
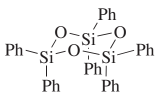
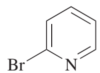
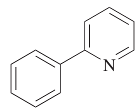
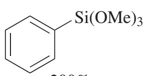
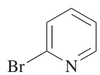
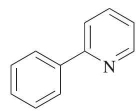
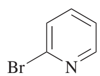
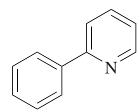
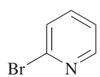
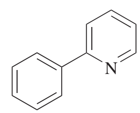
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 13 h		(93)	151
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(94)	47
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 90°, 24 h		(70)	236
200%		$PdCl_2$ (5%), TBAF•$3H_2O$ (200%), toluene, 100°, 10 h		(50)	237
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h		(73)	276

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O (1:1), reflux, 22 h	 (69)	265
 125%		TBAF•$3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 23 h	 (86)	47
 20%		$Pd(OAc)_2$ (5%), KOH (880%), dioxane/H_2O, reflux, 8 h	 (70)	265
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 90°, 24 h	 (76)	236
120%		$Pd(dba)_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•$3H_2O$ (120%), toluene, 80°, 18 h	 (73)	241
200%		$Pd(OAc)_2$ (3%), IPr•HCl (3%), TBAF (200%), 1,4-dioxane/THF (5:2), 80°, 7 h	 (81)	244

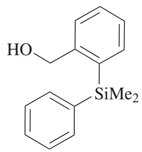
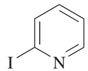
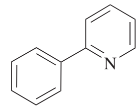
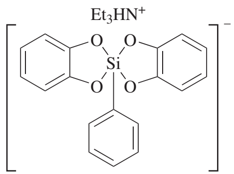
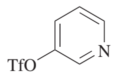
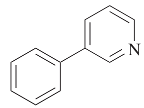
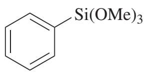
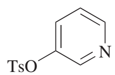
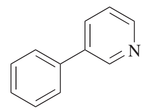
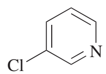
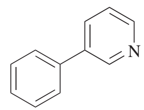
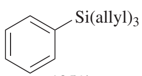
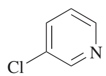
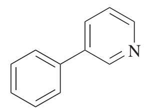
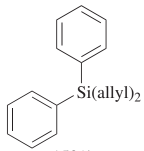
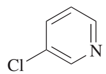
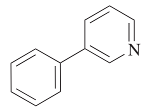
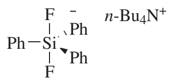
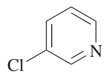
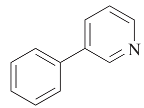
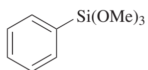
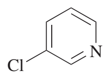
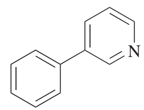
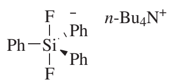
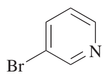
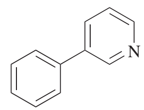
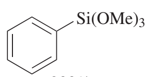
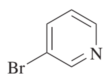
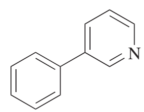
 116%		$PdCl_2$ (3%), CuI (10%), **L4** (4%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 13 h	 (96)	151
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h	 (78)	276
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF, 80°	 (31)	249
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h	 (72)	245
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h	 (98)	47

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		TBAF•$3H_2O$ (600%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (25:1), 80°, 7 h	 (95)	47
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (56)	269
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h	 (58)	247
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (92)	269
 200%		$Pd(OAc)_2$ (10%), PPh_3 (20%), TBAF (200%), DMF, 90°, 24 h	 (62)	236

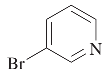
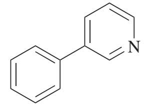
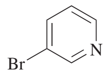
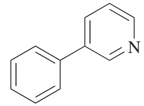
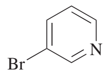
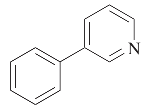
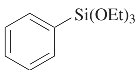
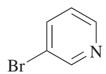
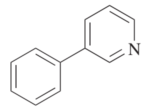
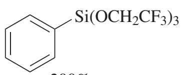
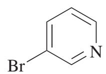
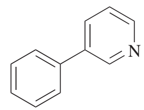
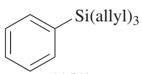
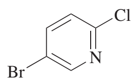
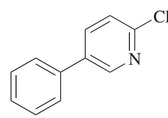
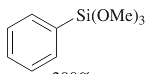
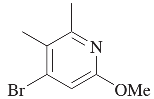
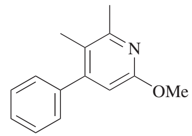
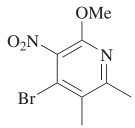
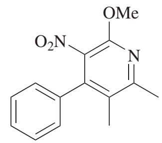
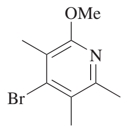
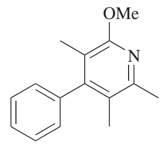
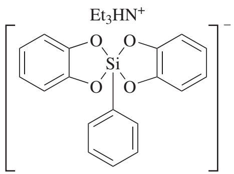
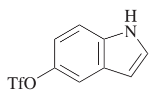
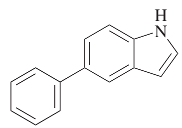
120%		Pd(dba)$_2$ (3%), *i*-Pr-DPEphos (4%), TBAF•3H_2O (120%), toluene, 80°, 18 h		(81)	241
200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h		(92)	247
200%		Pd cat. **2** (7%), TBAF (250%), H_2O, 135–140°, 24 h		(99)	245
 150%		Pd(NH$_3$)$_2$Cl$_2$ (0.5%), **L2** (0.5%), NaOH (200%), H_2O, 120°, 5 h		(67)	246
 200%		Pd(OAc)$_2$ (10%), PPh$_3$ (20%), TBAF (200%), DMF, 90°, 24 h		(62)	236
 115%		TBAF•3H_2O (460%), PdCl$_2$ (5%), PCy$_3$ (10%), DMSO/H_2O (10:1), 80°, 3 h		(89)	47

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h	 (97)	242, 243
200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h	 (36)	242, 243
200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF/THF, 80°, 12 h	 (89)	242, 243
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane, reflux, 6 h	 (69)	276

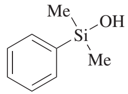
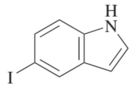
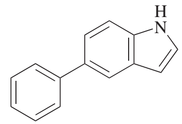
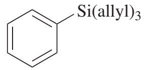
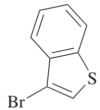
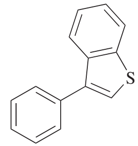
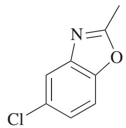
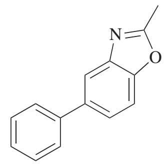
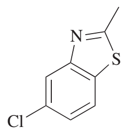
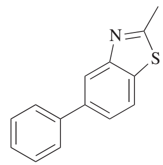
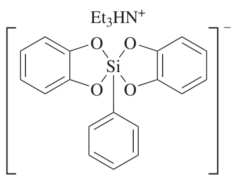
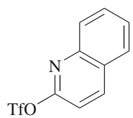
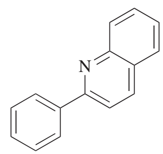
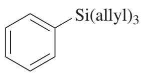
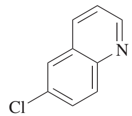
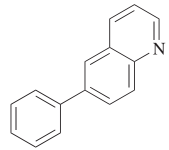
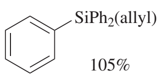
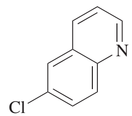
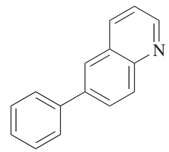
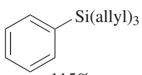
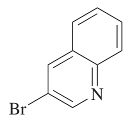
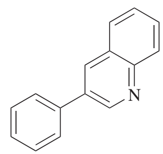
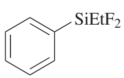
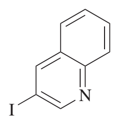
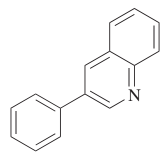
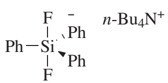
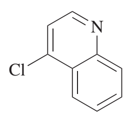
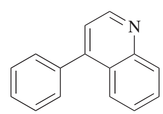
 120%		$Pd(PPh_3)_3$ (3%), Ag_2O (10%), TBAT (12%), THF, 70°, 0.5 h		(50)	201
 115%		$TBAF•3H_2O$ (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 5 h		(93)	47
125%		$TBAF•3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h		(83)	47
125%		$TBAF•3H_2O$ (500%) , $[allylPdCl]_2$ (2.5% eq), XPhos (10%), THF/H_2O (20:1), 80°, 12 h		(84)	47
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h		(91)	276

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 125%		TBAF•$3H_2O$ (500%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 14 h	 (99)	47
 105%		TBAF•$3H_2O$ (330%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (40:1), 80°, 7 h	 (96)	47
 115%		TBAF•$3H_2O$ (460%), $[allylPdCl]_2$ (5%), XPhos (10%), THF/H_2O (20:1), 80°, 2 h	 (97)	47
 150%		$[allylPdCl]_2$ (2.5%), KF (200%), DMF, 100°, 12 h	 (68)	172
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h	 (70)	269

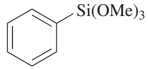
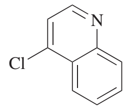
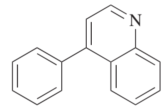
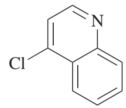
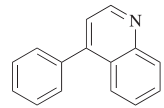
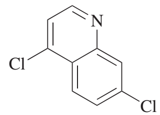
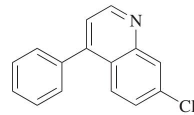
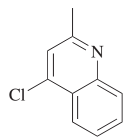
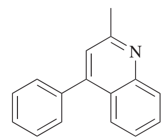
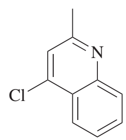
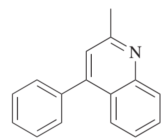
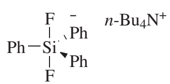
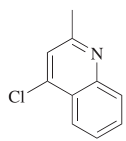
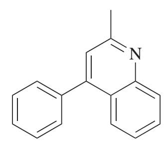
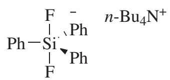
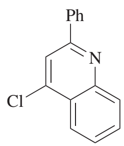
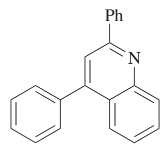
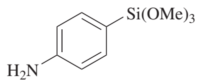
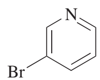
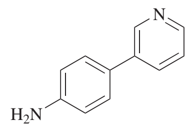
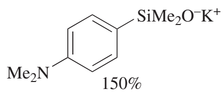
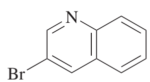
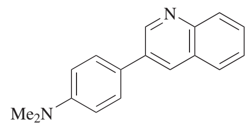
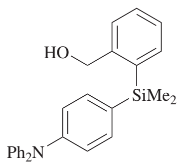
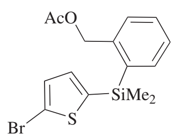
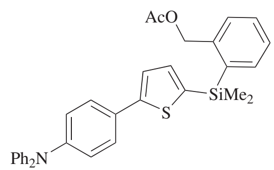
 200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF, 80°, 24 h		(88)	247
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(88)	245
200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h		(75)	247
200%		Pd cat. **2** (7%), TBAF (200%), MeCN/THF (5:1), 80°, 24 h		(89)	247
200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(81)	245
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(73)	269

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 200%		Pd cat. **1** (10%), NaOH (0.5 M, 1 mL), toluene/H_2O (6:1), 135–140°, 24 h		(72)	269
 200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(77)	245
 150%		(t-$Bu_3P)_2Pd$ (2.5%), toluene, 90°, 3 h		(80)	54
 120%		$[allylPdCl]_2$ (1.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 7 h		(81)	149

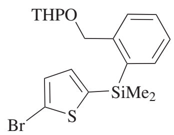
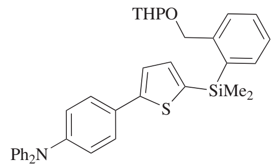
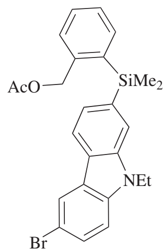
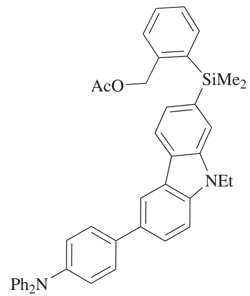
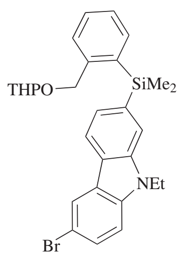
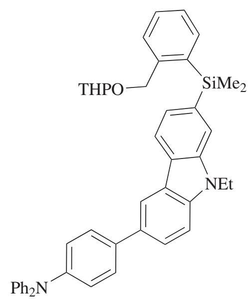
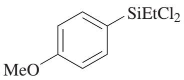
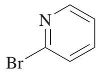
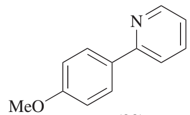
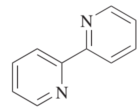
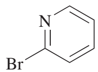
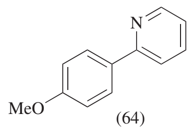
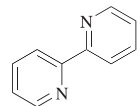
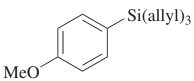
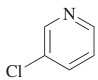
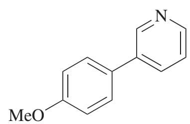
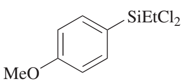
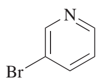
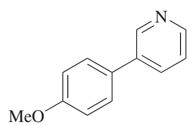
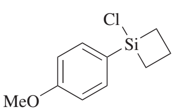
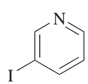
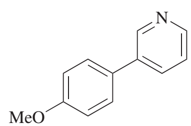
120%		$[allylPdCl]_2$ (1.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 8 h		(81)	149
150%		$[allylPdCl]_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 18 h		(94)	149
120%		$[allylPdCl]_2$ (0.5%), CuI (3%), RuPhos (2.1%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 22 h		(85)	149

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-tol})_3$ (0.5%), KF (200%), DMF, 120°, 18 h	 (23) +  (63)	73
120–160%		$Pd(OAc)_2$ (0.5–1%), PPh_3 (1–2%), NaOH (600%), THF, 60°, 39 h	 (64) +  (—)	185
 120%		TBAF $3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 6 h	 (92)	47
 120%		$Pd(OAc)_2$ (0.5%), $P(o\text{-tol})_3$ (0.5%), KF (2 eq), DMF, 120°, 18 h	 (69)	73
 120%		TBAF (360%), $[allylPdCl]_2$ (2.5%), $(t\text{-Bu})_3P$ (20%), THF, reflux, 5 h	 (71)	39

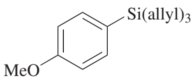
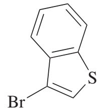
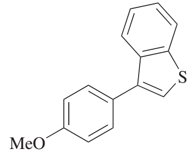
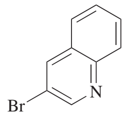
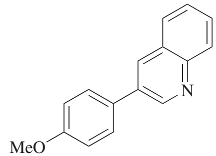
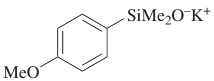
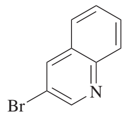
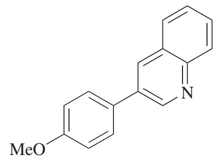
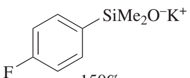
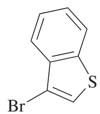
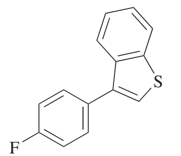
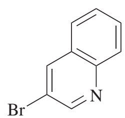
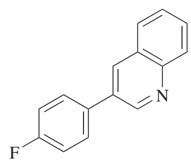
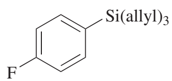
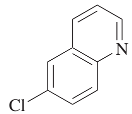
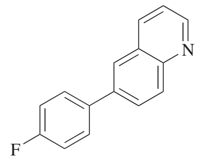
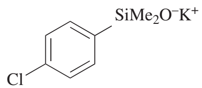
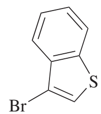
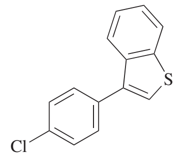
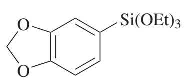
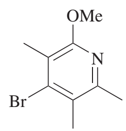
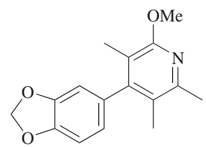
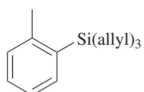
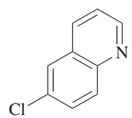
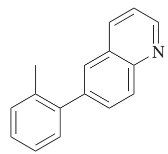
 115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 5 h	 (87)	47
115%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 4 h	 (95)	47
 150%		(t-$Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h	 (85)	54
 150%		(t-$Bu_3P)_2Pd$ (2.5%), toluene, 90°, 5 h	 (65)	54
150%		(t-$Bu_3P)_2Pd$ (2.5%), toluene, 90°, 5 h	 (84)	54

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 180%		TBAF•$3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 13 h	 (98)	47
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 3.5 h	 (61)	54
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h	 (61)	243
C_7				
 130%		TBAF•$3H_2O$ (480%), $[allylPdCl]_2$ (2.5%), XPhos (10%), THF/H_2O (20:1), 80°, 7 h	 (87)	47

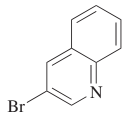
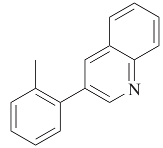
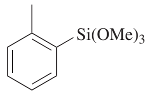
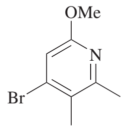
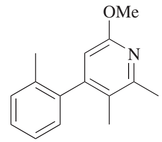
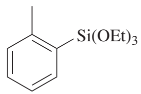
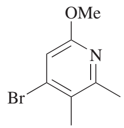
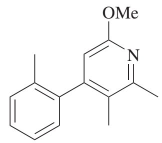
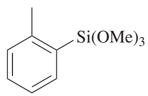
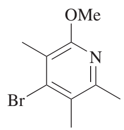
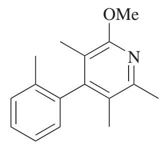
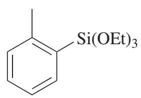
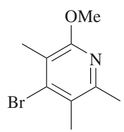
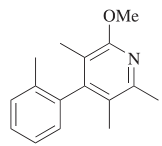
130%		TBAF•3H_2O (460%), $PdCl_2$ (5%), PCy_3 (10%), DMSO/H_2O (10:1), 80°, 20 h		(80)	47
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h		(10)	242
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h		(10)	243
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF 80°, 12 h		(10)	242
 200%		$Pd(OAc)_2$ (20%), PPh_3 (40%), TBAF (200%), DMF, 80°, 12 h		(10)	243

TABLE 1B. CROSS-COUPLING OF ARYLSILANES WITH HETEROARYL ELECTROPHILES *(Continued)*

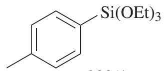
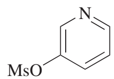
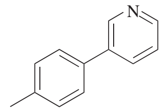
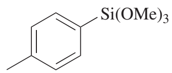
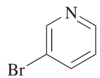
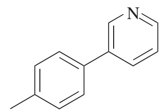
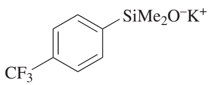
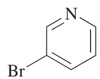
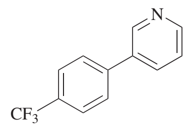
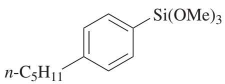
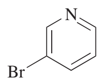
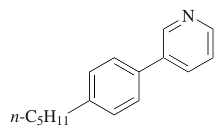
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 200%		$Pd(OAc)_2$ (4%), XPhos (10%), TBAF (200%), THF/*t*-BuOH, 90°		(40)	248
 200%		Pd cat. **2** (7%), NaOH (250%), H_2O, 135–140°, 24 h		(92)	245
 150%		$(t\text{-}Bu_3P)_2Pd$ (5%), toluene, 90°, 5 h		(78)	54
C_{11}					
	 120%	1. TBAF (105%) 2. $Pd(OAc)_2$ (5%), Ph_3P (15%), toluene, reflux, 30 h		(72)	240

TABLE 1C. CROSS-COUPLING OF ARYLSILANES WITH ALKENYL ELECTROPHILES

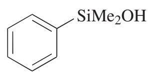
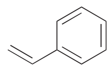
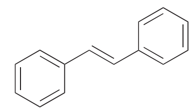
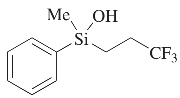
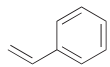
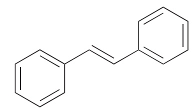
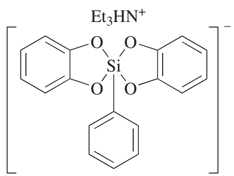
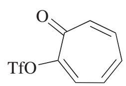
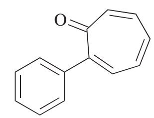
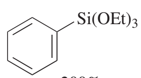
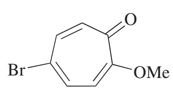
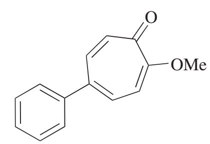
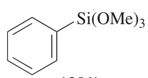
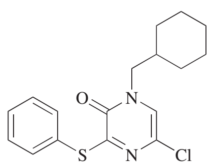
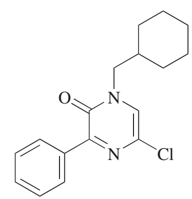
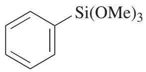
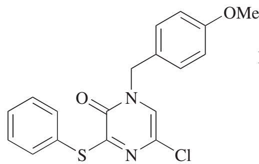
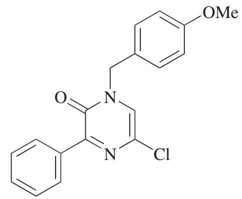
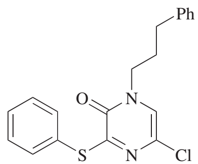
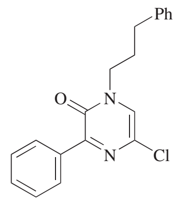
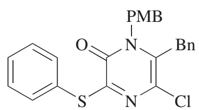
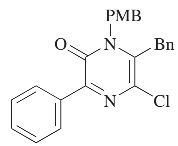
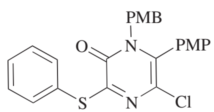
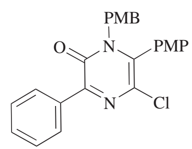
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h	 (63)	277
		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 3 h	 (59)	203
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), THF, reflux, 6 h	 (89)	276
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h	 (84)	251
 120%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1 h	 (90)	252

TABLE 1C. CROSS-COUPLING OF ARYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 110%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 3 h		(79)	252
120%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1 h		(89)	252
130%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1.5 h		(95)	252
110%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1.5 h		(90)	252

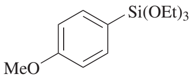
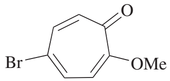
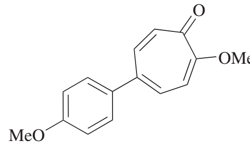
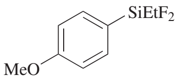
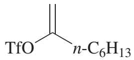
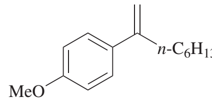
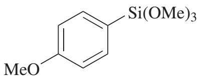
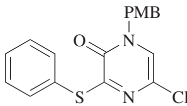
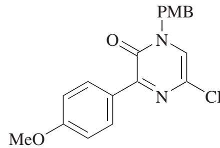
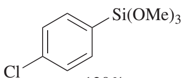
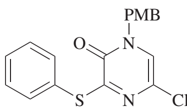
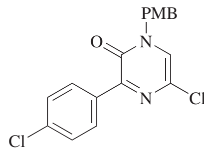
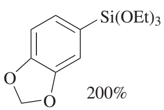
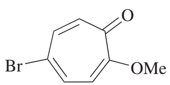
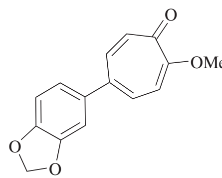
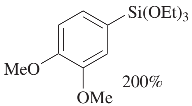
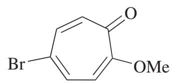
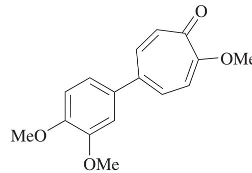
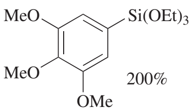
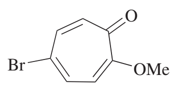
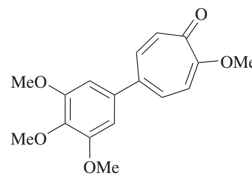
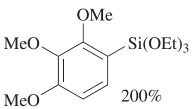
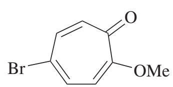
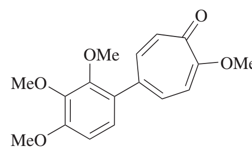
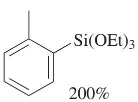
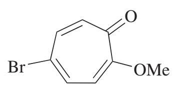
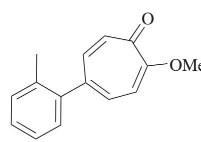
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h		(81)	251
 120%		$Pd(PPh_3)_4$ (3–5%), TBAF (120%), THF, 50°, 5 h		(62)	181
 110%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1 h		(98)	252
 120%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1 h		(89)	252
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h		(81)	251

TABLE 1C. CROSS-COUPLING OF ARYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h	 (88)	251
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h	 (89)	251
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h	 (92)	251
C_7				
 200%		$Pd(OAc)_2$ (10%), PPh_3 (50%), TBAF (200%), THF, 12 h	 (81)	251

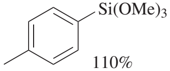
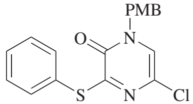
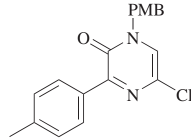
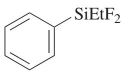
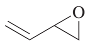
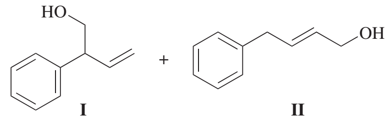
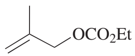
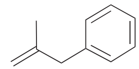
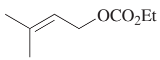
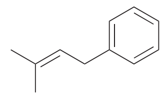
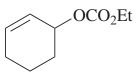
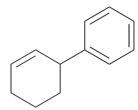
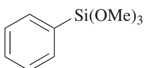
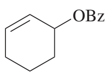
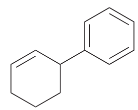
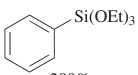
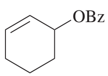
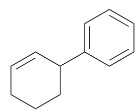
 110%		$Pd(PPh_3)_4$ (5%), CuI (100%), TBAF (200%), THF, 60°, 1 h		(89)	252

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 40°	 **I** **II** **I** + **II** (68), **I**:**II** = 1:2	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), DMF, 60°, 19 h	 (52)	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°, 19 h	 (33)	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), DMF, 60°, 19 h	 (40)	175
 200%		$Pd(dba)_2$, TBAF, DMF, 85°	 (100)	70
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 50°, 14 h	 (95)	253

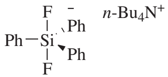
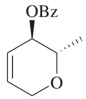
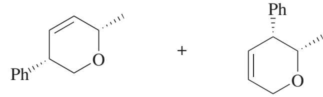
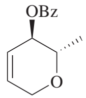
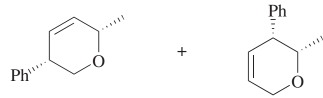
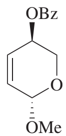
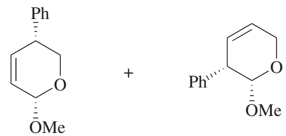
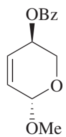
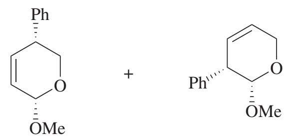
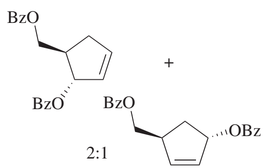
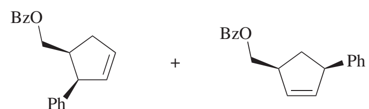
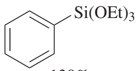
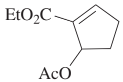
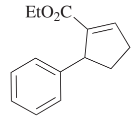
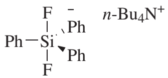
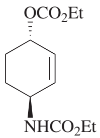
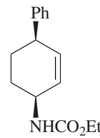
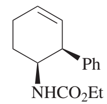
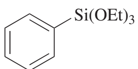
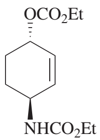
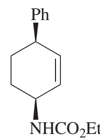
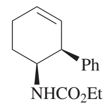
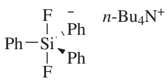
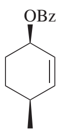
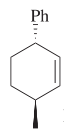
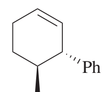
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 50°, 14 h	 **I** + **II** **I** + **II** (60), **I**:**II** = 15:1	316
200%		$Pd(dba)_2$ (8.5%), dppe (8.5%), THF, reflux, 12 h	 **I** + **II** **I** + **II** (61), **I**:**II** = 1:1	316
200–400%		$Pd(dba)_2$ (8.5%), dppe (8.5%), THF, reflux, 12 h	 **I** + **II** **I** + **II** (73), **I**:**II** = 15:1	316
200–400%		$Pd(dba)_2$ (5%), PPh_3 (5%), THF, reflux, 12 h	 **I** + **II** **I** + **II** (75), **I**:**II** = 1:1	316
200%	 2:1	$Pd(dba)_2$ (5.4%), PPh_3 (5.4%), THF, reflux, 12 h	 **I** + **II** **I** + **II** (42), **I**:**II** = 1:20	111

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, 50°	 (48)	255
 200%		$Pd_2(dba)_3$•$CHCl_3$ (5%), PPh_3 (10%), THF, 55°	 +  **I** **I** + **II** (53), **I**:**II** = 1:1 **II**	111
 200%		$Pd_2(dba)_3$•$CHCl_3$ (5%), PPh_3 (10%), THF, 48 h	 +  **I** **I** + **II** (51), **I**:**II** = 1:1 **II**	111
 200%		$Pd(dba)_2$ (10%), PPh_3 (10%), THF, 75°, 17 h	 **I** +  **II** **I** + **II** (94), **I**:**II** = 1:2	111

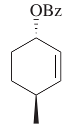
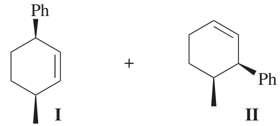
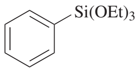
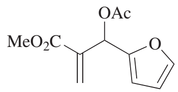
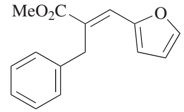
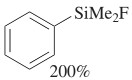
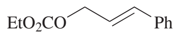
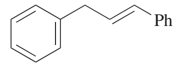
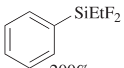
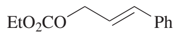
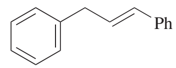
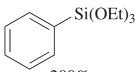
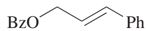
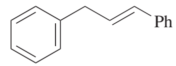
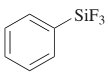
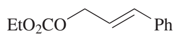
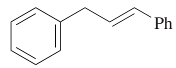
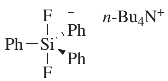
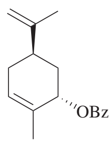
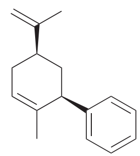
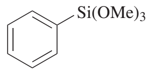
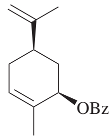
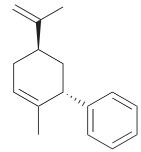
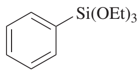
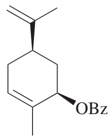
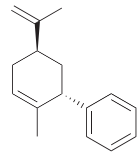
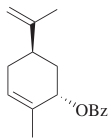
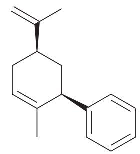
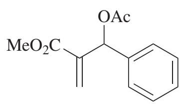
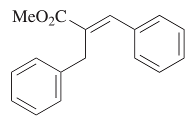
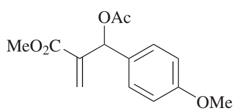
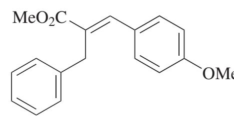
200%		$Pd(dba)_2$ (10%), PPh_3 (10%), THF, 75°, 17 h	 **I** + **II** (91), **I**:**II** = 10:1	111
 130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (78) (*E*)/(*Z*) = 99:1	255
 200%		$Pd_2(dba)_3$•$3CHCl_3$ (2.5%), PPh_3 (5%), benzene, rt, 20 h	 (90) (*E*)/(*Z*) = 99:1	175
 200%		$Pd_2(dba)_3$•$3CHCl_3$ (2.5%), PPh_3 (5%), benzene, 40°, 4 h	 (91)	175
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 12 h	 (95)	253
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°, 19 h	 (73)	175
 200%		$Pd(dba)_2$ (5%), PPh_3 (5%), THF, reflux, 12 h	 (60)	316

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		$Pd(dba)_2$, TBAF, DMF, 85°	 (81)	70
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 50°, 14 h	 (83)	253
200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 54°, 14 h	 (84)	253
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (92) (*E*)/(*Z*) = 93:7	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (94) (*E*)/(*Z*) = 99:1	255

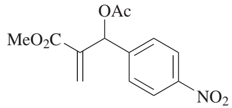
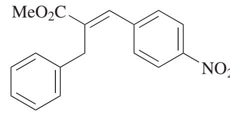
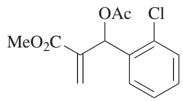
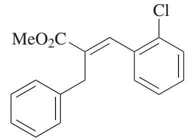
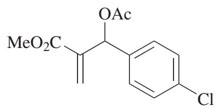
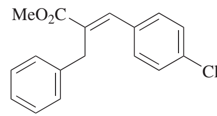
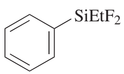
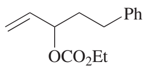
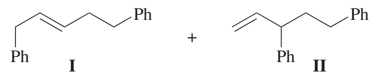
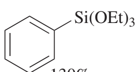
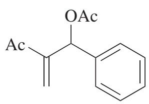
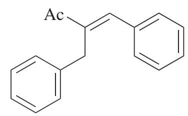
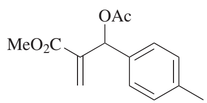
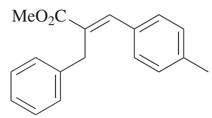
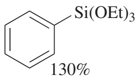
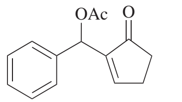
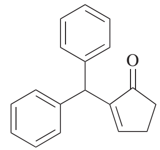
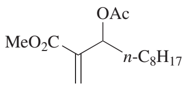
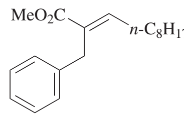
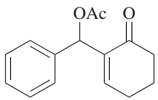
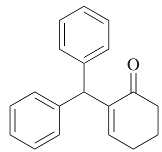
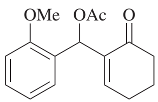
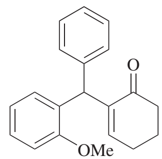
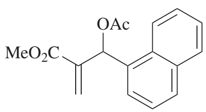
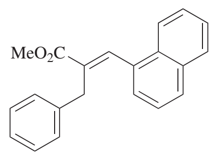
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h		(62) (*E*)/(*Z*) = 96:4	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h		(86) (*E*)/(*Z*) = 92:8	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h		(91) (*E*)/(*Z*) = 99:1	255
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°, 19 h	 **I** + **II** (93), **I**:**II** = 10:1		175
 130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 6 h		(90)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h		(89) (*E*)/(*Z*) = 95:5	255

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (51)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (85) (*E*)/(*Z*) = 90:10	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (70)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (61)	111
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (87) (*E*)/(*Z*) = 96:4	255

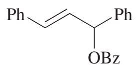
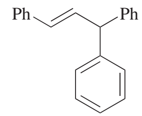
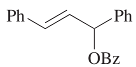
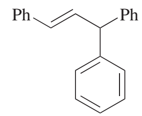
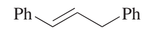
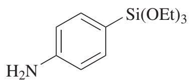
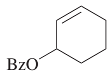
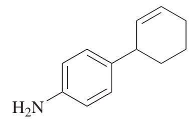
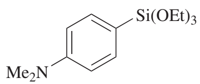
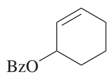
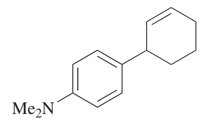
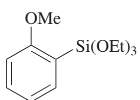
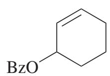
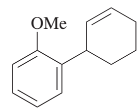
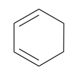
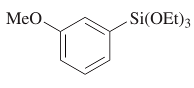
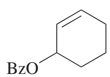
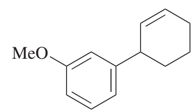
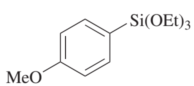
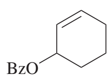
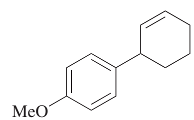
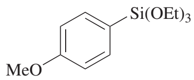
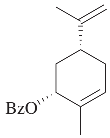
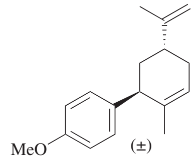
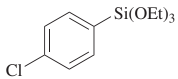
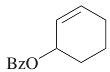
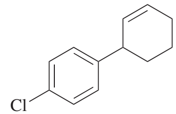
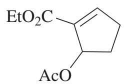
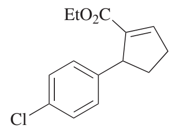
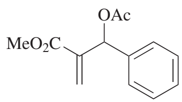
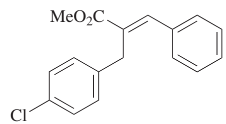
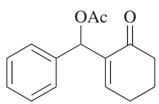
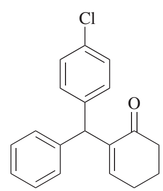
200%		$Pd(dba)_2$ (10%), TBAT (200%), PPh_3 (10%), THF, reflux, 36 h	 (55)	253
200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, reflux, 14 h	 (25) +  (25)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 55°, 14 h	 (34)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 55°, 14 h	 (84)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 14 h	 (9) +  (50)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 12 h	 (88)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 15 h	 (88)	253

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 20 h	 (78)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 12 h	 (87)	253
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, 50°	 (48)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (92) (*E*)/(*Z*) = 98:2	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (77)	255

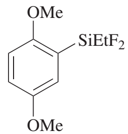
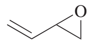
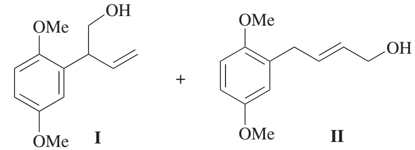
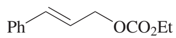
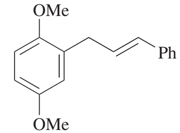
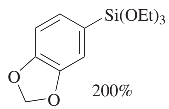
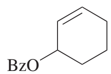
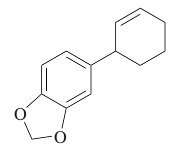
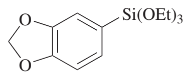
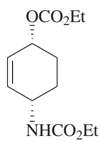
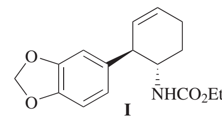
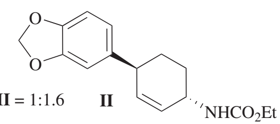
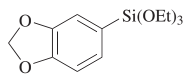
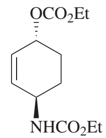
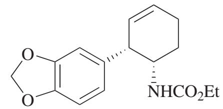
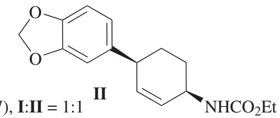
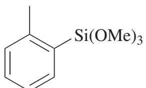
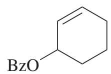
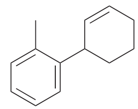
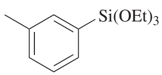
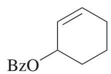
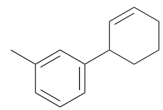
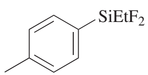
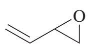
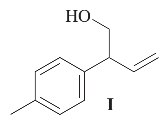
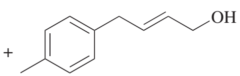
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°	 **I** + **II** (51), **I**:**II** = 1:1	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°, 19 h	 (97)	175
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 14 h	 (87)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 65°	 +  **I** + **II** (81), **I**:**II** = 1:1.6	317

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 200%		$Pd(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, 55°, 20 h	 **I** +  **II** **I** + **II** (67), **I**:**II** = 1:1	111
C_7				
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 15 h	 (77)	253
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 10 h	 (86)	253
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°	 **I** +  **II** **I** + **II** (65), **I**:**II** = 1:2.5	253

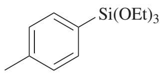
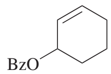
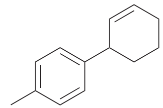
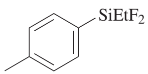
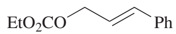
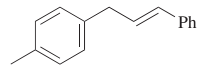
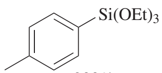
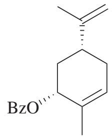
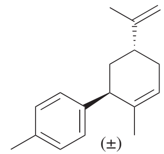
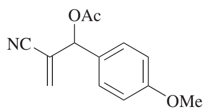
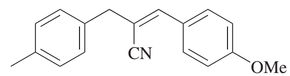
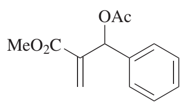
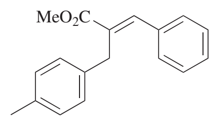
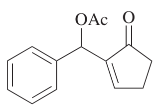
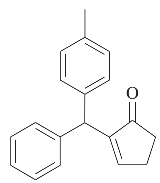
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 12 h	 (87)	253
 200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), PPh_3 (5%), benzene, 60°, 19 h	 (85)	175
 200%		$Pd(dba)_2$ (10%), TBAF (200%), THF, 60°, 48 h	 (±) (84)	253
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, 50°, 5 h	 (54)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 3 h	 (86) (*E*)/(*Z*) = 97:3	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (53)	255

TABLE 1D. CROSS-COUPLING OF ARYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

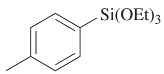
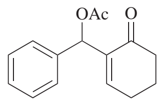
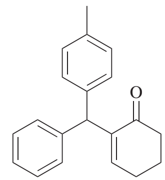
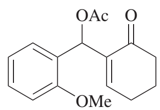
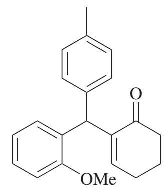
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (66)	255
130%		$Pd_2(dba)_3$ (3%), TBAF (200%), PEG, rt, 8 h	 (61)	255

TABLE 1E. CROSS-COUPLING OF ARYLSILANES WITH ALKYL ELECTROPHILES

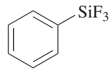
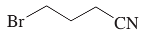
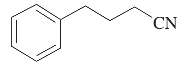
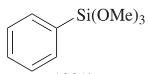
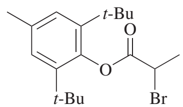
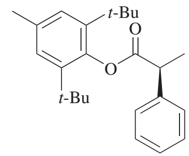
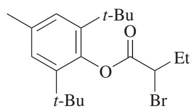
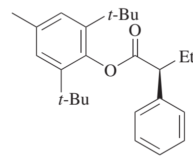
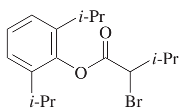
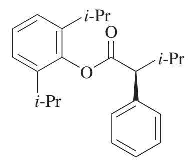
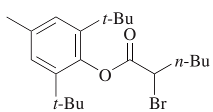
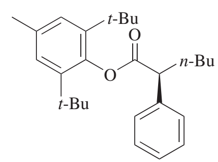
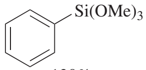
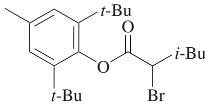
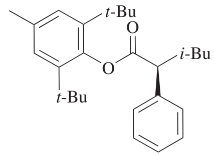
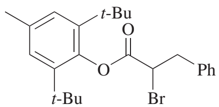
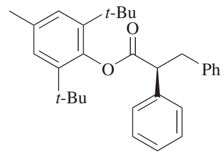
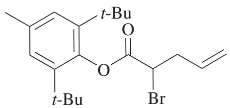
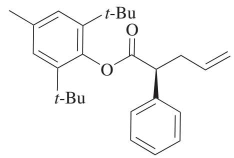
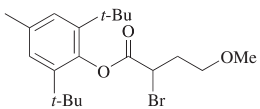
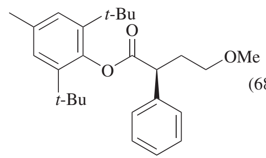
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (73)	189
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (84) 89% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (80) 99% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (72) 75% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (76) 92% ee	118

TABLE 1E. CROSS-COUPLING OF ARYLSILANES WITH ALKYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (64) 93% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (72) 84% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (78) 80% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (68) 99% ee	118

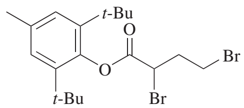
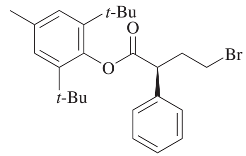
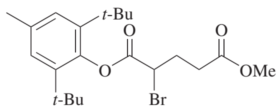
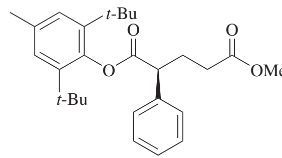
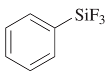
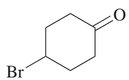
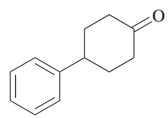
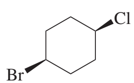
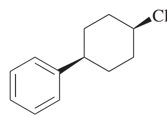
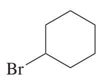
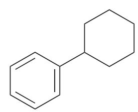
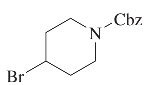
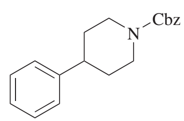
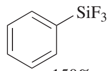
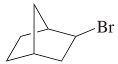
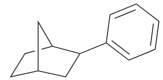
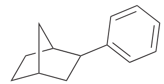
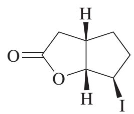
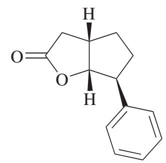
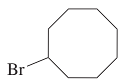
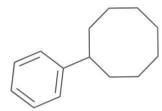
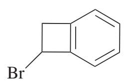
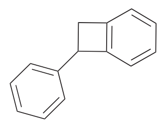
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (70) 86% ee	118
130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h	 (80) 92% ee	118
 150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (82)	189
150%	 *cis/trans* = 95:5	$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (60) *cis/trans* = 55:45	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (80)	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (63)	189

TABLE 1E. CROSS-COUPLING OF ARYLSILANES WITH ALKYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%	 *exo*/*endo* = 96:4	$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (62) *exo*/*endo* = 94:6	189
150%	 *exo*/*endo* = 6:94	$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (70) *exo*/*endo* = 95:5	189
150%	 *exo* only	$NiBr_2$•diglyme (9%), BPhen (10%), CsF (380%), DMSO, 60°, 20 h	 (60) *exo* only	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (62)	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h	 (80)	189

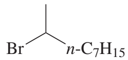
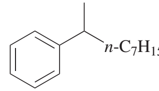
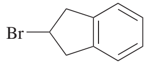
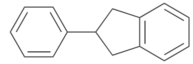
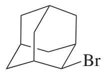
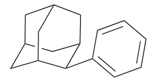
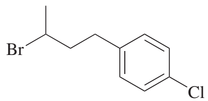
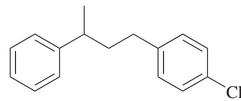
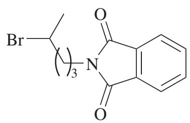
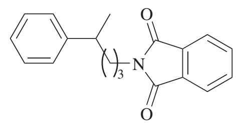
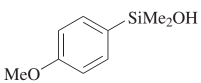
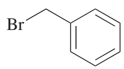
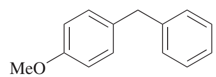
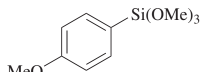
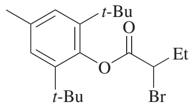
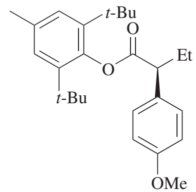
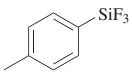
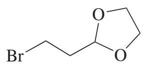
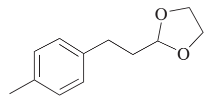
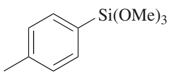
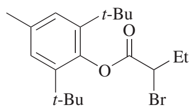
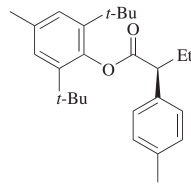
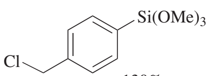
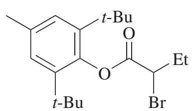
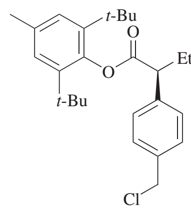
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h		(65)	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h		(71)	189
150%		$NiBr_2$•diglyme (9%), BPhen (10%), CsF (380%), DMSO, 60°, 20 h		(68)	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h		(72)	189
150%		$NiBr_2$•diglyme (6.5%), BPhen (10%), CsF (380%), DMSO, 60°, 20 h		(70)	189
 120%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), THF, 60°, 36 h		(55)	37

TABLE 1E. CROSS-COUPLING OF ARYLSILANES WITH ALKYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h		(64) 87% ee	118
C_7					
 150%		$NiBr_2$•diglyme (6.5%), BPhen (7.5%), CsF (380%), DMSO, 60°, 20 h		(80)	189
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h		(76) 92% ee	118
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h		(72) 94% ee	118

C_{10}

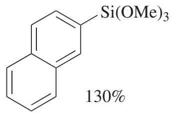
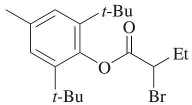
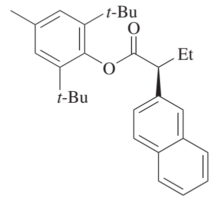
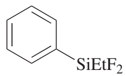
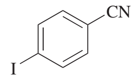
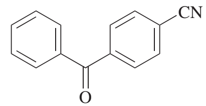
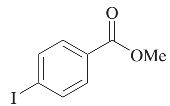
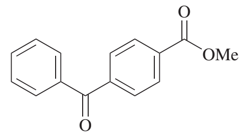
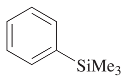
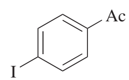
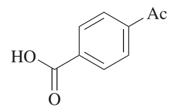
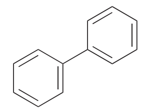
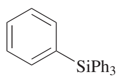
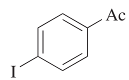
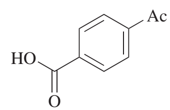
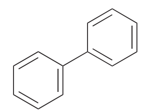
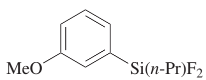
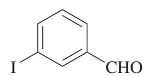
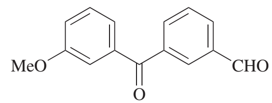
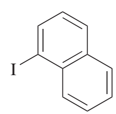
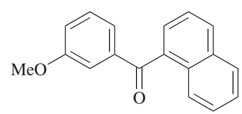
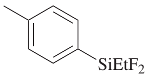
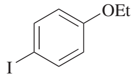
 130%		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt, 16 h		(74) 89% ee	118

TABLE 1F. CARBONYLATIVE CROSS-COUPLING OF ARYLSILANES WITH MISCELLANEOUS ELECTROPHILES

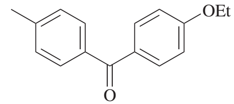
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 150%		$[allylPdCl]_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 5 h	 (60)	179, 182
150%		$[allylPdCl]_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 5 h	 (61)	179, 182
 150%		$[allylPdCl]_2$ (2.5%), KF (165%), CO (1 atm), DMI, 100°, 12 h	 (52) +  (14)	179
 150%		$[allylPdCl]_2$ (2.5%), KF (165%), CO (1 atm), DMI, 100°, 12 h	 (49) +  (23)	179
 150%		$[allylPdCl]_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 5 h	 (80)	179, 182
150%		$[allylPdCl]_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 15 h	 (67)	179, 182

C_7

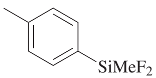

150%

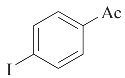


[allylPdCl]$_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 19 h

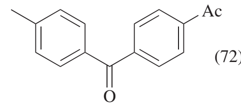

(69)

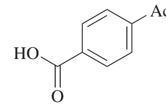
182


150%

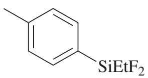


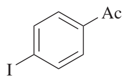
[allylPdCl]$_2$ (2.5%), KF (165%), CO (1 atm), DMI, 100°, 12 h


(72) +

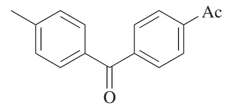

(20)

179

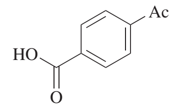

150%



Pd cat. (2.5%), KF (*x*%), CO (1 atm), solvent, 100°

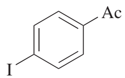

I

+

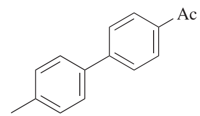

II

Pd cat.	*x*	Solvent	Time (h)	**I**	**II**	
[allylPdCl]$_2$	165	DMF	48	(41)	(—)	179
$PdCl_2(PPh_3)_2$	165	DMI	12	(34)	(46)	179
$Pd(PPh_3)$	165	DMI	12	(51)	(43)	179
[allylPdCl]$_2$	165	DMI	12	(—)	(64)	179
[allylPdCl]$_2$	110	DMI	3	(91)	(—)	179, 182

150%

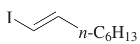


[allylPdCl]$_2$ (2.5%), KF (165%), CO (1 atm), DMI, 150°, 1 h

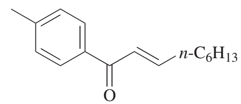

(73)

179

150%



[allylPdCl]$_2$ (2.5%), KF (150%), CO (1 atm), DMI, 50°, 25 h


(58)

179

TABLE 1F. CARBONYLATIVE CROSS-COUPLING OF ARYLSILANES WITH MISCELLANEOUS ELECTROPHILES (*Continued*)

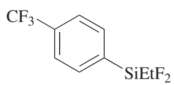
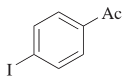
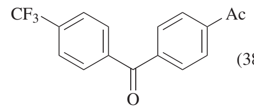
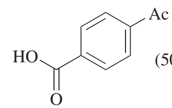
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 150%		$[allylPdCl]_2$ (2.5%), KF (110%), CO (1 atm), DMI, 100°, 18 h	 (38) +  (50)	179, 182

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES

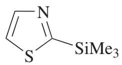
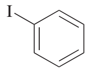
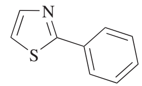
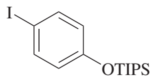
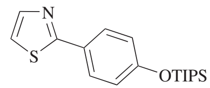
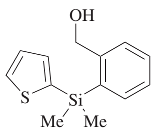
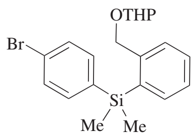
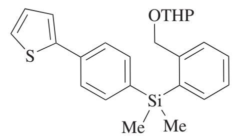
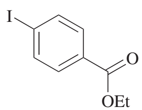
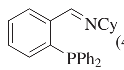
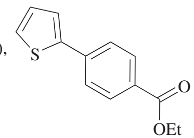
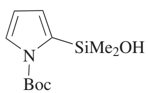
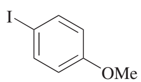
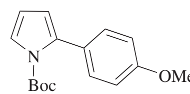
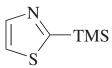
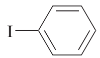
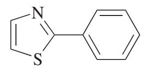
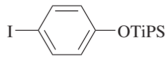
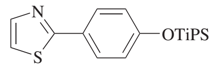
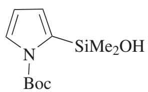
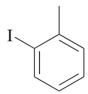
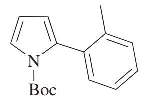
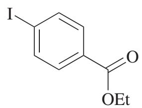
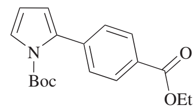
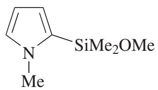
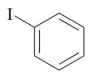
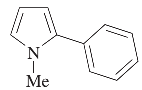
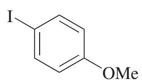
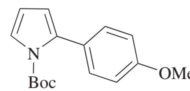
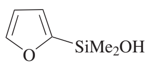
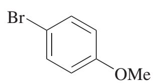
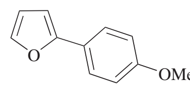
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 50%	CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h	 (93)	231
	 50%	CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h	 (87)	231
C_4				
 120%		Pd(dppf)Cl_2•CH_2Cl_2 (3%), CuI (3%), K_2CO_3 (250%), THF/DMF (3:1), 50°, 6 h	 (96)	149
		$PdCl_2$ (3%),  (4%), CuI (10%), K_2CO_3 (200%), H_2O (200%), DMSO, 50°, 10 h	 (93)	151
 120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 36 h	 (72)	207, 208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_3					
		CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h		(9)	231
		CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h		(8)	231
C_4					
 120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(80)	207, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(76)	207, 208
	 50%	CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h		(93)	231
		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 36 h		(72)	207, 208
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 6 h		(66)	207, 208

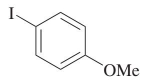
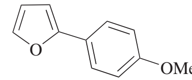
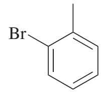
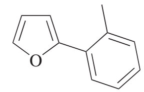
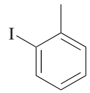
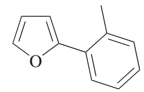
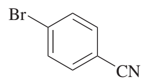
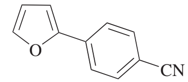
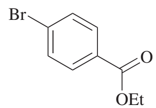
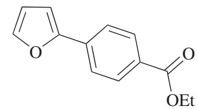
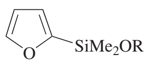
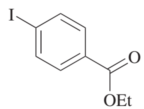
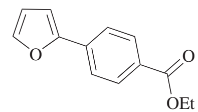
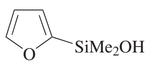
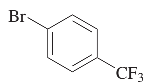
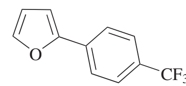
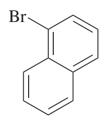
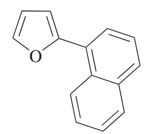
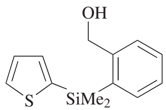
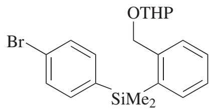
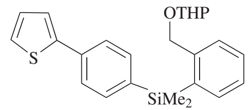
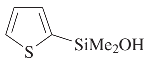
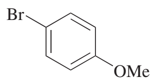
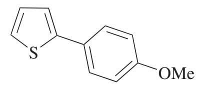
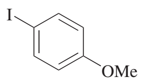
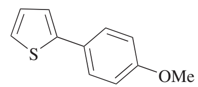
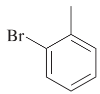
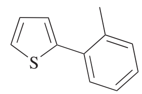
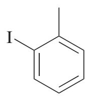
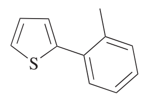
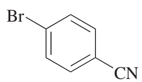
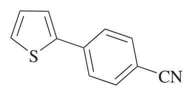
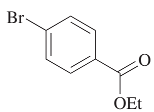
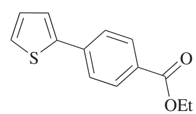
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), furyl$_3$As (20%), toluene, 50°, 24 h		(71)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(71)	207, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(61)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(73)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(60)	207, 208
 120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 1 h		R Na (79)[a] H (82)	207, 208
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(71)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 6 h		(69)	207, 208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_4					
		$Pd(dppf)Cl_2\ CH_2Cl_2$ (3%), CuI, K_2CO_3 (250%), THF/DMF (3:1), 50°, 6 h		(96)	285
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(71)	207, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 80°, 24 h		(72)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(77)	207, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(79)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(78)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h		(67)	207, 208

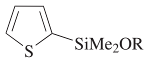
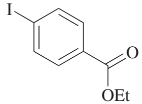
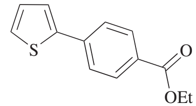
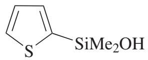
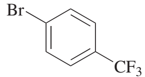
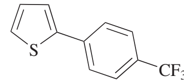
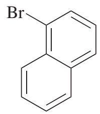
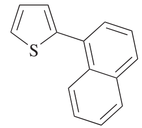
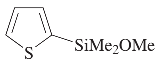
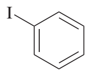
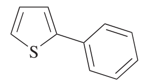
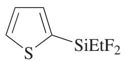
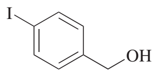
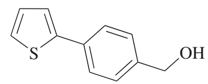
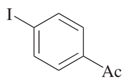
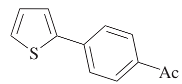
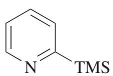
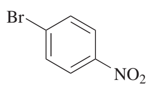
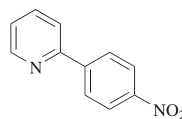
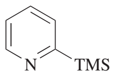
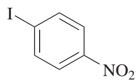
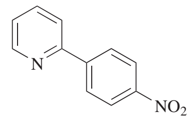
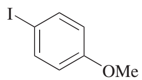
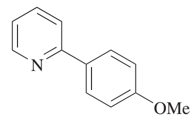
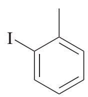
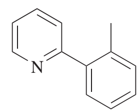
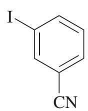
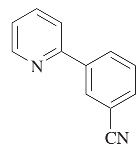
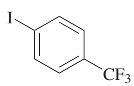
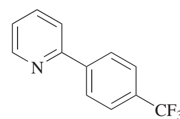
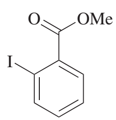
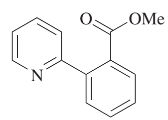
 120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 1–3 h		R: Na (87)[a]; H (78)	207, 208
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 3 h	 (86)	207, 208
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 7 h	 (74)	207, 208
	 50%	CuI (100%), C_6F_5ONa (200%), DMI, 130°, 12 h	 (75)	231
 150%		$[allylPdCl]_2$ (2.5%), KF (200%), DMF, 100°, 64 h	 (81)	172
150%		$[allylPdCl]_2$ (2.5%), KF (200%), DMF, 100°, 64 h	 (96)	172
C_5				
 300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (67)	122

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
 300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (75)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (45)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (21)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (65)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (50)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°	 (48)	122

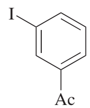
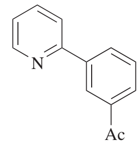
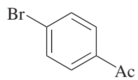
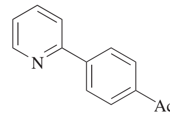
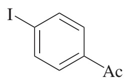
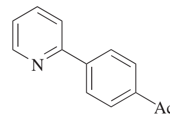
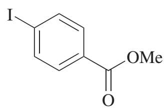
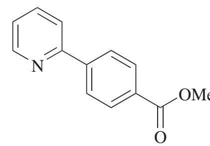
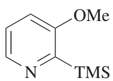
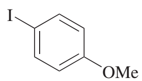
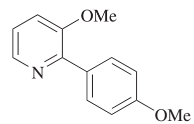
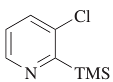
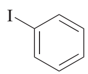
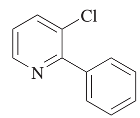
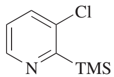
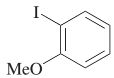
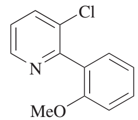
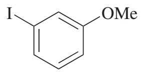
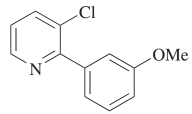
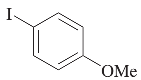
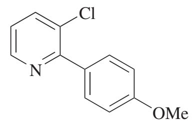
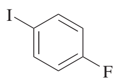
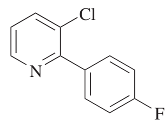
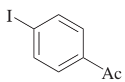
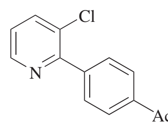
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°		(61)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°		(40)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°		(47)	122
300%		$Pd(PPh_3)_4$ (5%), Ag_2O (100%), TBAF (10%), DMF, 90°		(47)	122
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(85)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(72)	123

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5					
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, 120°, 12 h		(38)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(55)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(82)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(88)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(80)	123

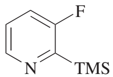
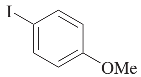
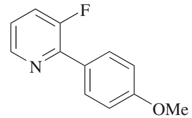
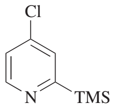
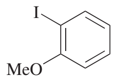
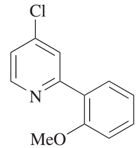
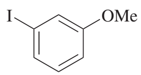
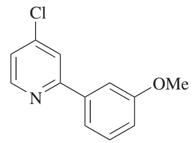
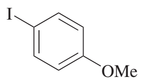
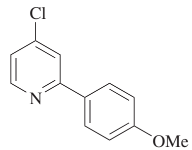
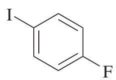
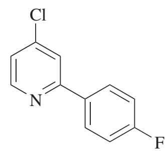
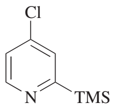
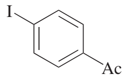
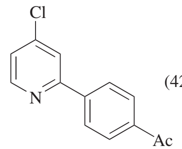
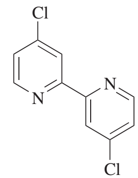
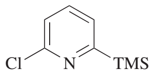
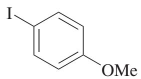
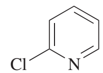
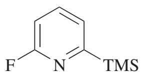
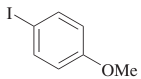
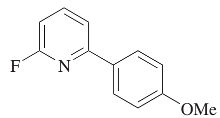
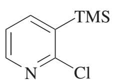
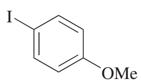
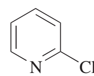
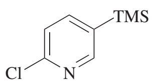
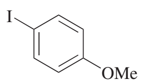
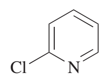
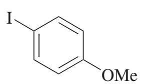
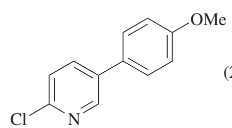
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(75)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(57)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(77)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(82)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(95)	123

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h	 (42) +  (40)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h	 (—)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h	 (64)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h	 (—)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h	 (—)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, 120°, 48 h	 (20)	123

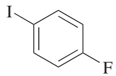
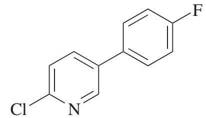
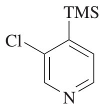
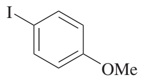
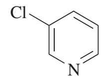
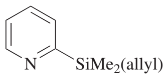
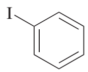
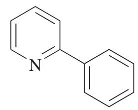
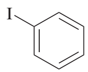
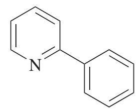
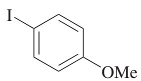
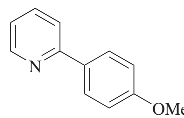
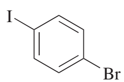
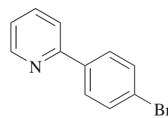
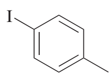
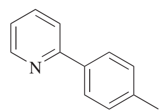
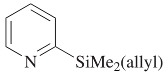
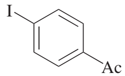
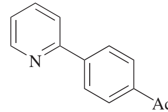
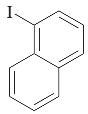
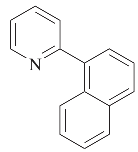
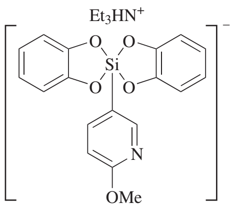
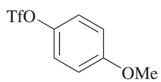
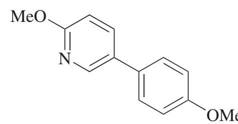
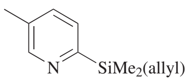
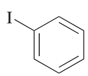
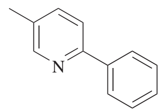
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (10%), DMF, rt, 24 h	 (—)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (10%), DMF, rt, 12 h	 (—)	123
 150%		$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°	 (60)	51
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°	 (78)	51
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°	 (72)	51
150%		$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°	 (81)	51
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°	 (93)	51

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5					
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°		(59)	51
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°		(76)	51
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane		(96)	276
C_6					
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°		(80)	51

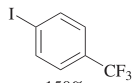
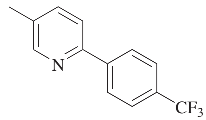
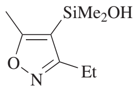
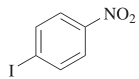
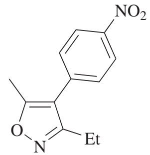
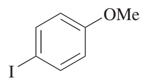
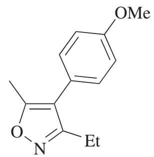
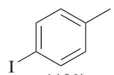
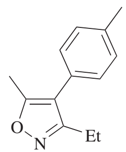
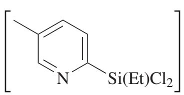
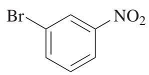
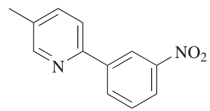
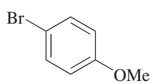
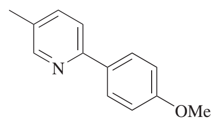
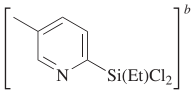
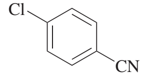
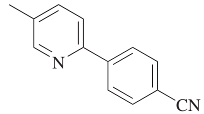
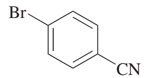
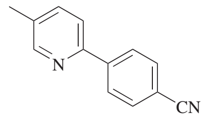
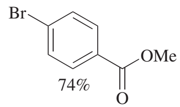
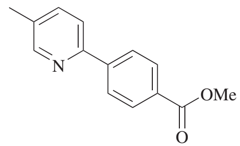
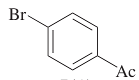
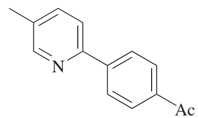
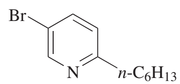
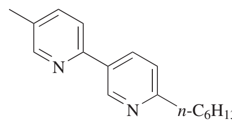
	 150%	$Pd(PPh_3)_4$ (5%), Ag_2O (150%), THF, 60°		(81)	51
	 110%	$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (100%), toluene, 40°		(57)	213
	 125%	$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (25%), toluene, 80°		(52)	213
	 110%	$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (25%), toluene, 80°		(56)	213
 [b]	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(80)	30
	 74%	$PdCl_2(PPh_3)_2$ (5%) KF, DMF, 120°, 48 h		(84)	30

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(81)	30
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(92)	30
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(73)	30
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(75)	30
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 72 h		(82)	30

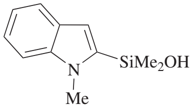
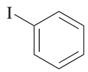
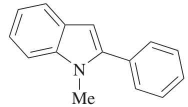
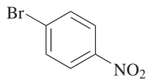
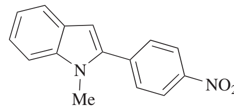
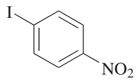
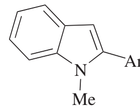
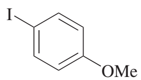
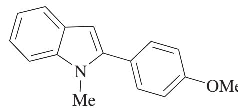
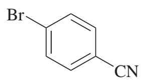
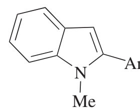
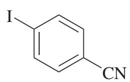
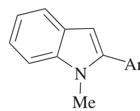
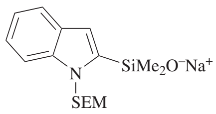
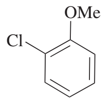
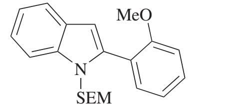
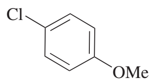
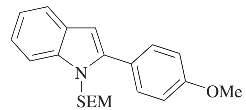
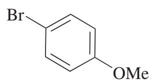
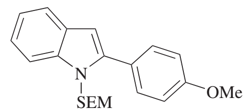
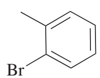
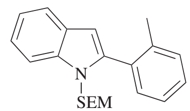
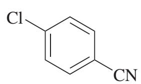
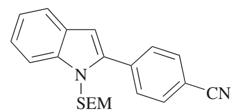
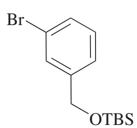
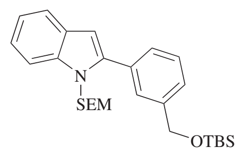
C_8  120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, rt, 3 h	 (82)	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), dppb (20%), CuI (100%), NaO*t*-Bu (200%), toluene, 55°, 20 h	 (84) + Ar—Ar (5) Ar = 4-$O_2NC_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (100%), NaO*t*-Bu (200%), toluene, rt, 3 h	 (62) + Ar—Ar (16) Ar = 4-$O_2NC_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (100%), NaO*t*-Bu (200%), toluene, rt, 3 h	 (80)	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), dppb (20%), CuI (100%), NaO*t*-Bu (200%), toluene, 55°, 20 h	 (80) + Ar—Ar (5) Ar = 4-NCC_6H_4	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (100%), NaOt-Bu (200%), toluene, rt, 3 h	 (62) + Ar—Ar (32) Ar = 4-NCC_6H_4	206, 208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
 120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 3 h		(94)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 3 h		(94)	208
120%		Pd cat. **4** (2.5%), toluene, 50°		(93)	208
120%		Pd cat. **4** (2.5%), toluene, 50°		(89)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 1 h		(92)	208
120%		Pd cat. **4** (2.5%), toluene, 50°		(83)	208

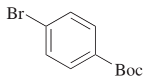
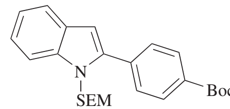
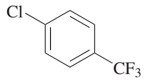
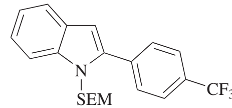
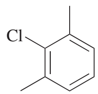
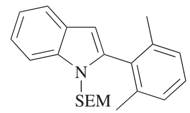
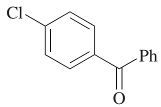
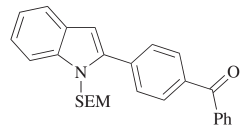
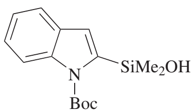
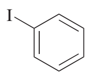
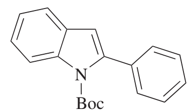
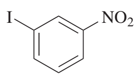
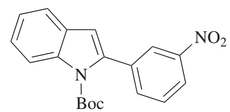
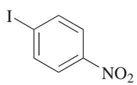
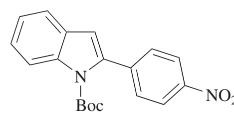
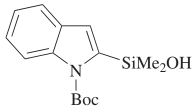
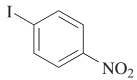
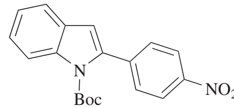
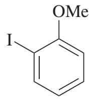
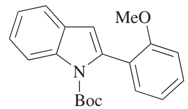
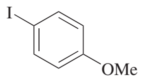
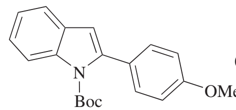
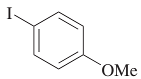
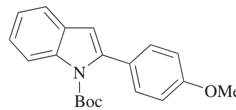
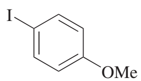
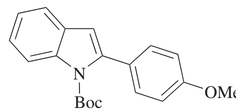
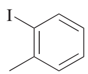
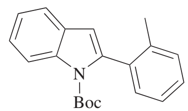
120%		Pd cat. **4** (2.5%), toluene, 50°		(93)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 1 h		(92)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 3 h		(88)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 1 h		(93)	208
 120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 40°, 12 h		(70) + Ph—Ph (12)	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 40°, 12 h		(72) + Ar—Ar (14) Ar = 3-$O_2NC_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, rt, 6 h		(84) + Ar—Ar (6) Ar = 4-$O_2NC_6H_4$	206, 208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaHMDS (120%), toluene, rt	 (93)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 50°, 24 h	 (75) + Ar—Ar (15) Ar = 2-$MeOC_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 50°, 24 h	 (72) + Ar—Ar (14) Ar = 4-$MeOC_6H_4$	206, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 80°, 3 h	 (68)	207, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaHMDS (120%), toluene, rt	 (62)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 50º, 24 h	 (73) + Ar—Ar (14) Ar = 2-MeC_6H_4	206, 208

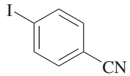
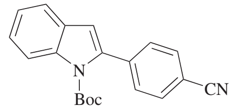
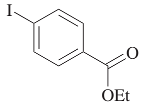
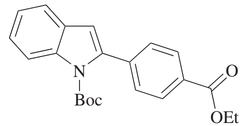
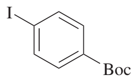
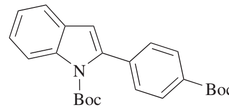
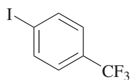
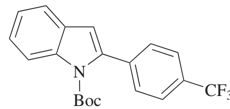
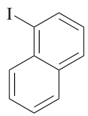
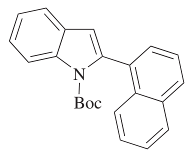
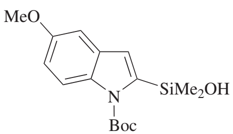
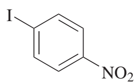
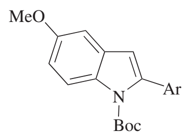
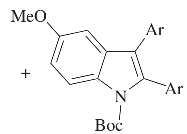
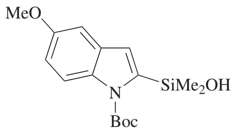
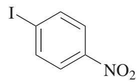
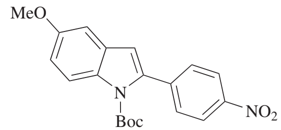
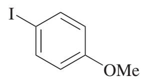
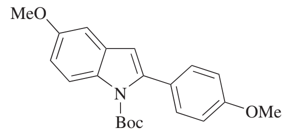
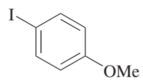
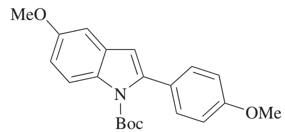
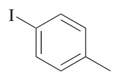
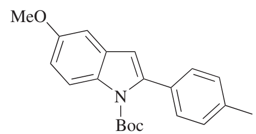
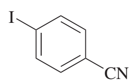
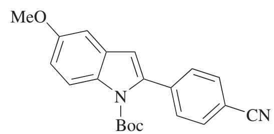
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h	 (81)	207, 208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h	 (82)	207, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, rt, 24 h	 (84) + Ar—Ar (trace) Ar = 4-$BocC_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, rt, 24 h	 (84) + Ar—Ar (3) Ar = 4-$CF_3C_6H_4$	206, 208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, 60°, 24 h	 (75) + Ar—Ar (13) Ar = 1-naphthyl	206
 120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), $Cu(OAc)_2$ (25%), toluene, rt, 3 h	 (72) +  (3) Ar = 4-$O_2NC_6H_4$	208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
 120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(80)	208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 24 h		(52)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaHMDS (120%), toluene, 40°, 12 h		(82)	208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 40°, 24 h		(68)	208
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(77)	208

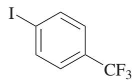
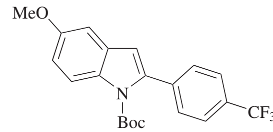
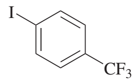
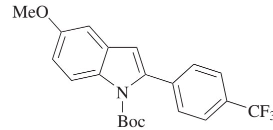
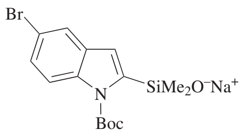
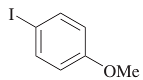
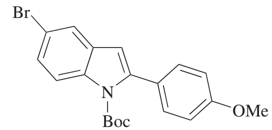
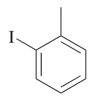
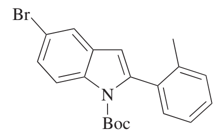
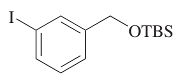
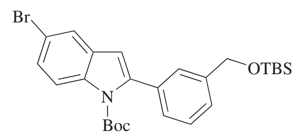
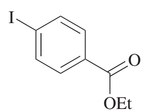
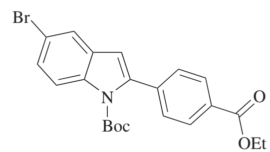
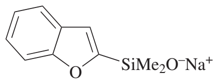
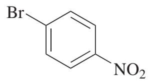
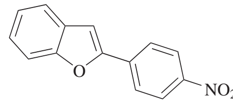
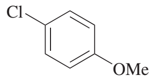
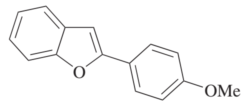
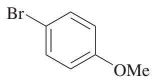
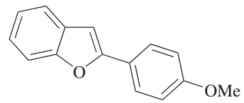
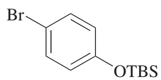
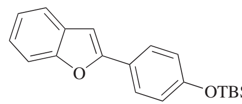
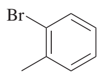
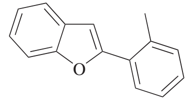
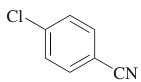
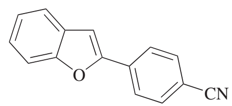
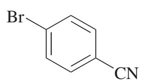
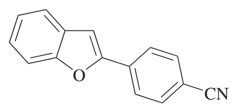
120%		1. NaH (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(87)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (200%), $Cu(OAc)_2$ (25%), toluene, rt, 4 h		(82)	208
 120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 80°, 24 h		(56)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 24 h		(54)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 80°, 24 h		(63)	208
120%		$Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 4 h		(85)	208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
 150%		$Pd(t\text{-}Bu_3P)_2$ (5%), THF, 60°, 8 h		(58)	54
150%		$[allylPdCl]_2$ (2.5%), SPhos (5%), THF, 60°, 3.5 h		(77)	54
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), toluene, 60°, 5 h		(82)	54
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), toluene, 60°, 5 h		(99)	54
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), toluene, 60°, 8 h		(95)	54
150%		$[allylPdCl]_2$ (2.5%), SPhos (5%), THF, 60°, 3.5 h		(64)	54
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), dioxane, 70°, 3.5 h		(59)	54

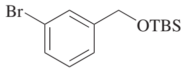
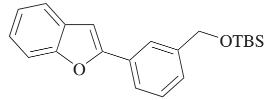
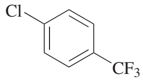
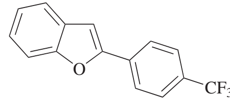
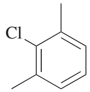
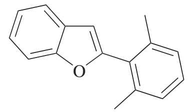
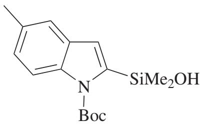
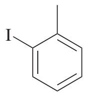
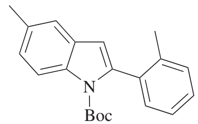
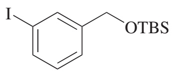
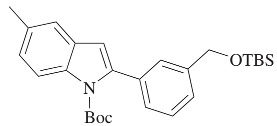
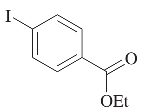
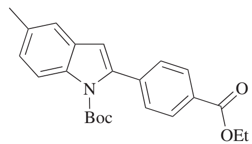
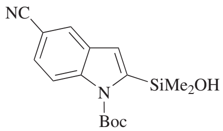
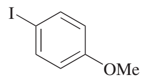
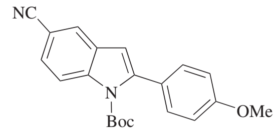
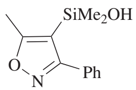
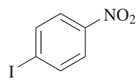
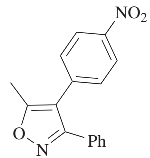
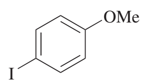
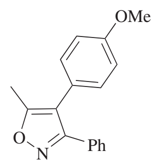
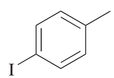
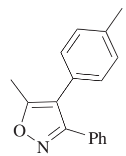
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), toluene, 60°, 5 h		(71)	54
150%		$[allylPdCl]_2$ (2.5%), SPhos (5%), THF, 60°, 3 h		(82)	54
150%		$[allylPdCl]_2$ (2.5%), SPhos (5%), THF, 60°, 5 h		(85)	54
C_9					
 120%		1. NaHMDS (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 3 h		(65)	208
120%		1. NaHMDS (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, 50°, 24 h		(76)	208
120%		1. NaHMDS (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 3 h		(82)	208

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_9					
 120%		1. NaHMDS (120%), toluene 2. $Pd_2(dba)_3$•$CHCl_3$ (5%), toluene, rt, 24 h		(70)	208
C_{10}					
 110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (100%), toluene, 40°		(63)	208
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), dioxane, 80°		(63)	213
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), dioxane, 80°		(75)	213

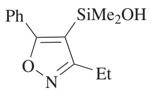
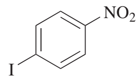
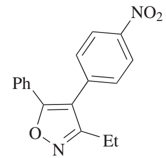
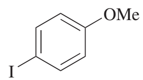
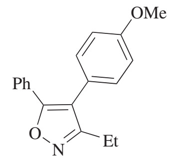
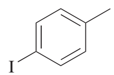
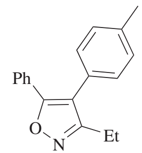
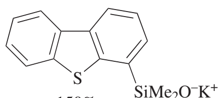
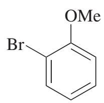
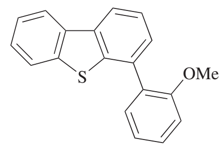
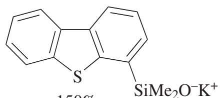
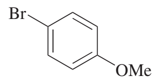
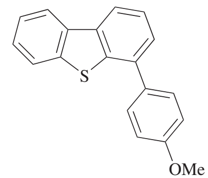
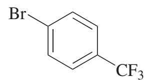
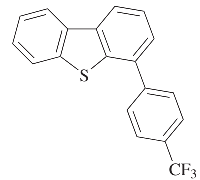
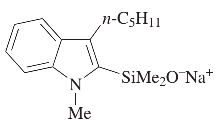
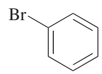
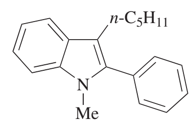
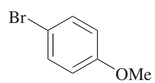
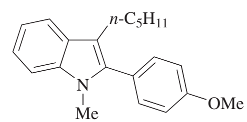
C_{11}					
 110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (100%), toluene, 40°		(78)	213
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (25%), toluene, 80°		(62)	213
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), $Cu(OAc)_2$ (25%), toluene, 80°		(61)	213
C_{12}					
 150%		$Pd(t\text{-}Bu_3P)_2$ (2.5%), toluene, 90°, 3 h		(89) (81)[c]	54

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}				
 150%		$Pd(t\text{-}Bu_3P)_2$ (2.5%), toluene, 90°, 3 h	 (96) (84)[c]	54
150%		$Pd(t\text{-}Bu_3P)_2$ (2.5%), toluene, 90°, 3 h	 (93)	54
C_{13}				
 120%		Pd cat. **4** (2.5%), toluene, 50°, 6 h	 (86)	209
120%		Pd cat. **4** (2.5%), toluene, 50°, 2 h	 (75)	209

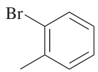
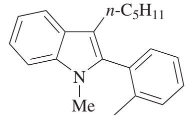
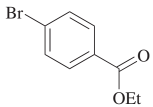
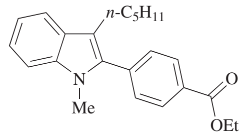
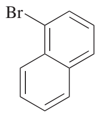
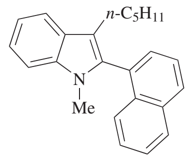
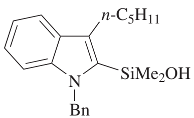
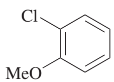
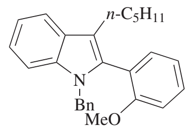
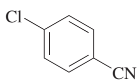
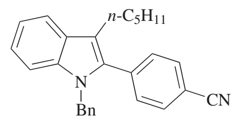
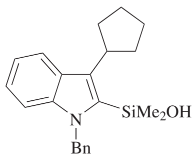
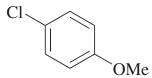
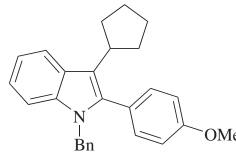
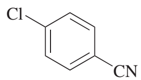
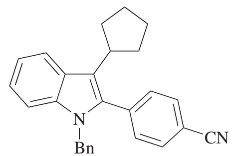
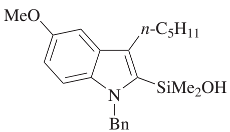
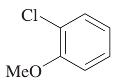
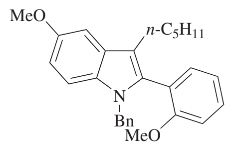
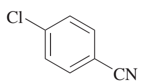
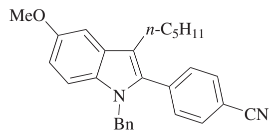
120%		Pd cat. **4** (2.5%), toluene, 50°, 12 h		(65)	209
120%		Pd cat. **4** (2.5%), toluene, 50°, 1 h		(73)	209
120%		Pd cat. **4** (2.5%), toluene, 50°, 3 h		(81)	209
 120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), Ru-Phos (5.0%), toluene, 70°, 12 h		(82)	209
120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), SPhos (5.0%), toluene, 70°, 1 h		(82)	209

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{13}					
 120%		1. NaH (120%), toluene 2. $[allylPdCl]_2$ (2.5%), RuPhos (5.0%), toluene, 90°, 12 h		(65)	209
120%		1. NaH (120%), toluene 2. $[allylPdCl]_2$ (2.5%), SPhos (5.0%), toluene, 70°, 1 h		(89)	209
 120%		1. NaH (120%), toluene 2. $[allylPdCl]_2$ (2.5%), RuPhos (5.0%), toluene, 70°, 24 h		(71)	209
120%		1. NaH (120%), toluene 2. $[allylPdCl]_2$ (2.5%), SPhos (5.0%), toluene, 70°, 1 h		(87)	209

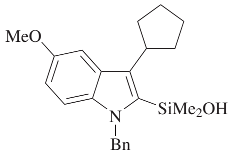
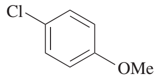
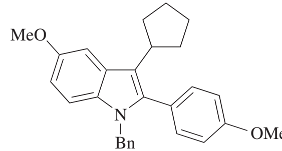
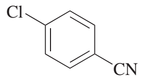
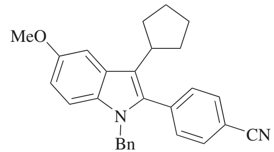
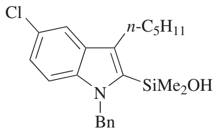
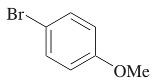
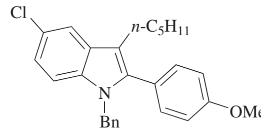
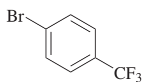
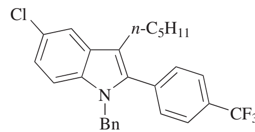
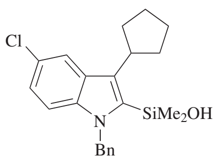
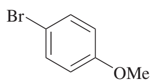
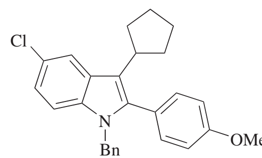
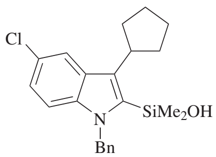
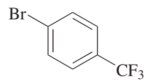
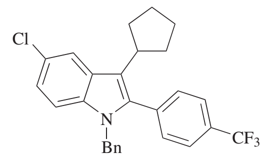
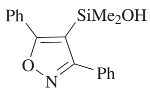
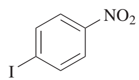
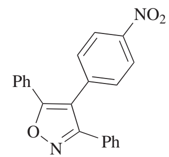
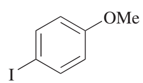
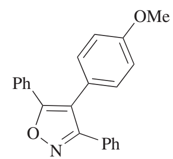
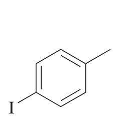
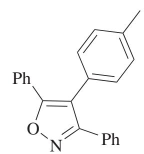
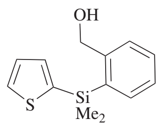
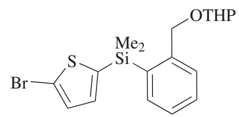
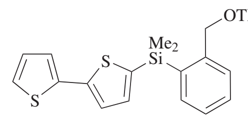
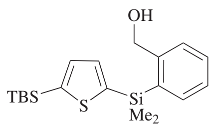
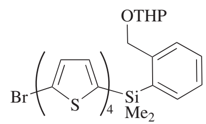
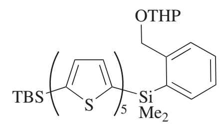
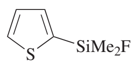
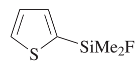
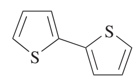
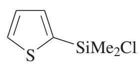
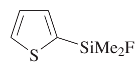
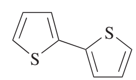
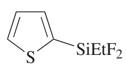
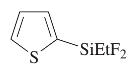
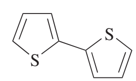
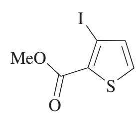
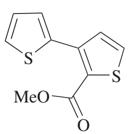
 120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), RuPhos (5.0%), toluene, 90°, 12 h	 (74)	209
120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), SPhos (5.0%), toluene, 70°, 1 h	 (88)	209
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 24 h	 (72)	209
120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 12 h	 (88)	209
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 12 h	 (62)	209

TABLE 2A. CROSS-COUPLING OF HETEROARYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{13}					
 120%		1. NaH (120%), toluene 2. Pd cat. **4** (2.5%), toluene, 50°, 12 h		(64)	209
C_{15}					
 110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), dioxane, 80°		(55)	213
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), dioxane, 80°		(68)	213
110%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaO*t*-Bu (250%), dioxane, 80°		(69)	213

[a] NaH is not needed when the sodium silanolate is used.
[b] The reactive silane is generated in situ from 2-bromo-5-methylpyridine, *n*-BuLi, and $EtSiCl_3$.
[c] This value is the yield of analytically pure material.

TABLE 2B. CROSS-COUPLING OF HETEROARYLSILANES WITH HETEROARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 120%		$Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (1%), CuI (3%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 6 h	 (96)	149
 120%		$Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (5%), CuI (5%), K_2CO_3 (250%), THF/DMF (3:1), 50°, 5 h	 (80)	149
		CuI (5%), TBAF (120%), MeCN, rt, 5 min	 (75)	178
		CuI (5%), TBAF (120%), MeCN, rt, 5 min	 (71)	178
		CuCl (100%), DMF, 60°, air, 3 h	 (78)	183
150%		$[allylPdCl]_2$ (2.5%), KF (200%), DMF, 100°, 12 h	 (82)	172

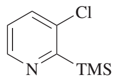
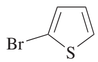
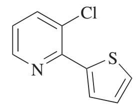
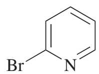
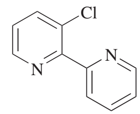
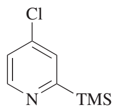
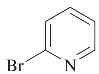
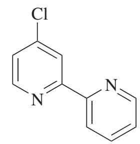
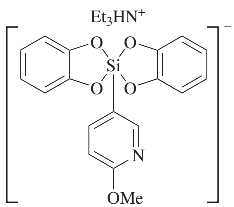
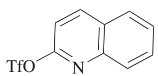
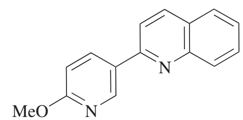
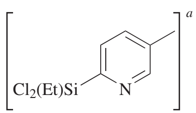
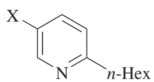
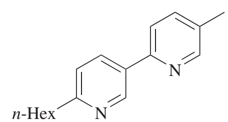
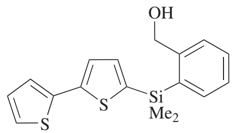
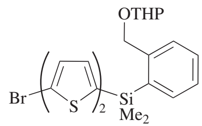
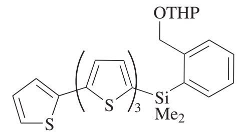
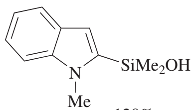
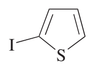
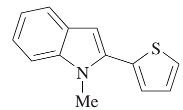
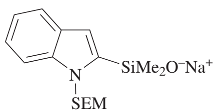
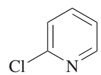
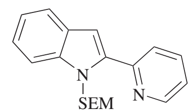
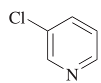
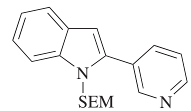
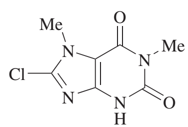
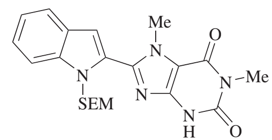
C_5					
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(78)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(65)	123
	 50%	$PdCl_2(PPh_3)_2$ (5%), Ph_3P (10%), CuI (100%), TBAF (200%), DMF, rt, 12 h		(85)	125
 150%		$Pd(dba)_2$ (5%), Cyclohexyl JohnPhos (5%), TBAF (150%), dioxane		(97)	276
C_6					
	 74%	$PdCl_2(PPh_3)_2$ (5%), KF, DMF, 120°, 48 h		(82)	30

TABLE 2B. CROSS-COUPLING OF HETEROARYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
 120%		$Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (3%), CuI (9%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 10 h		(82)	149
 120%		$Pd_2(dba)_3 \cdot CHCl_3$ (5%), NaO*t*-Bu (200%), CuI (100%), toluene, rt, 6 h		(73)	206, 208
 120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 90°, 3 h		(73)	208
		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 2 h		(84)	208
120%		$[allylPdCl]_2$ (2.5%), SPhos (5%), toluene, 70°, 3 h		(86)	208

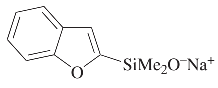
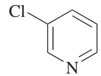
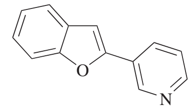
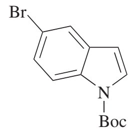
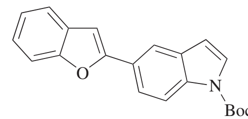
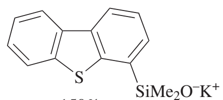
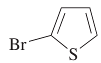
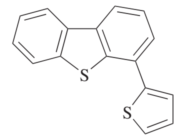
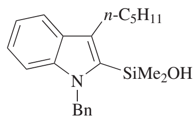
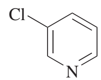
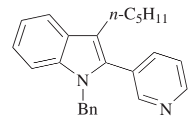
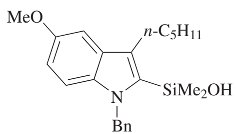
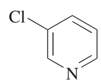
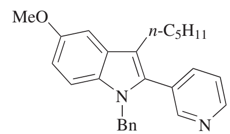
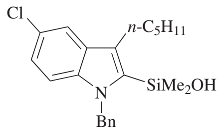
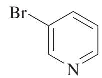
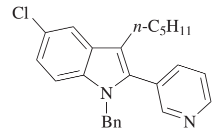
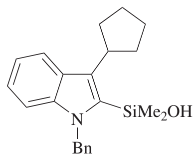
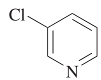
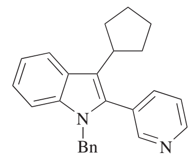
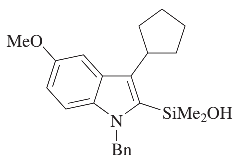
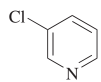
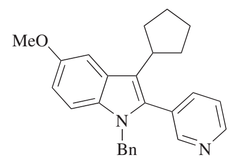
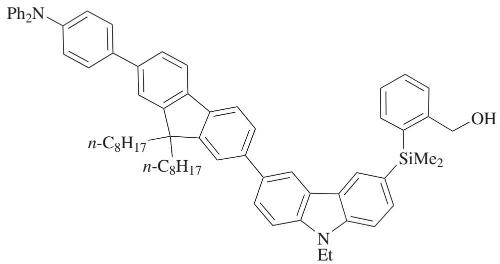
 150%		$[allylPdCl]_2$ (2.5%), SPhos (5%), THF, 60°, 6.5 h		(67)	54
150%		$Pd(t\text{-}Bu_3P)_2$ (5%), THF, 60°, 5 h		(91)	54
C_{12}					
 150%		$Pd(t\text{-}Bu_3P)_2$(2.5%), toluene, 90°, 3 h		(73) (65)[b]	54
C_{13}					
 120%		1. NaH, toluene 2. $[allylPdCl]_2$ (2.5%), RuPhos (5.0%), toluene, 70°, 12 h		(87)	209
 120%		1. NaH (120%), toluene 2. $[allylPdCl]_2$ (2.5%), RuPhos (5.0%), toluene, 70º, 1 h		(81)	209

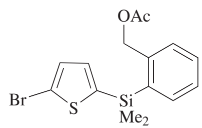
TABLE 2B. CROSS-COUPLING OF HETEROARYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{13}					
 120%		1. NaH, toluene 2. Pd cat. **4** (2.5%), toluene, 50º, 12 h		(88)	209
 120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), RuPhos (5.0%) toluene, 90º, 12 h		(69)	209
 120%		1. NaH (120%), toluene 2. [allylPdCl]$_2$ (2.5%), RuPhos (5.0%) toluene, 90º, 12 h		(86)	209

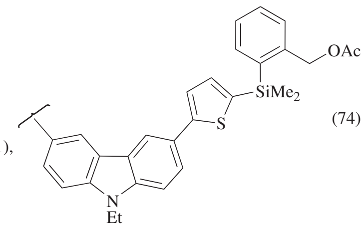
509

C_{47}



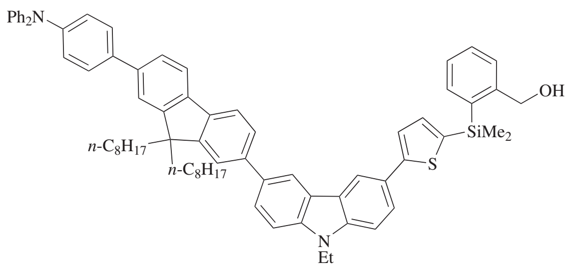
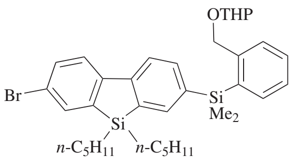
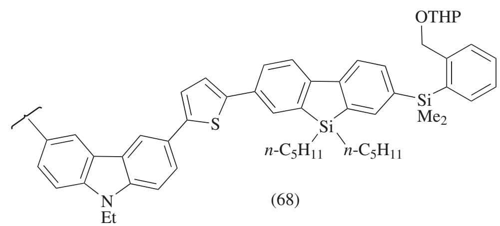


$[allylPdCl]_2$ (1%),
RuPhos (11%), CuI (3%),
K_2CO_3 (100%), THF/DMF (3:1),
75º, 24 h



(74) 149

TABLE 2B. CROSS-COUPLING OF HETEROARYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{51} 	 (*electrophile*)	Pd(dppf)Cl_2•CH_2Cl_2 (5%), CuI (5%), K_2CO_3 (250%), THF/DMF (3:1), 75°, 24 h	 (68)	149

[a] The starting silane was generated in situ from 2-bromo-5-methylpyridine.

[b] This value is the yield of analytically pure material.

TABLE 2C. CROSS-COUPLING OF HETEROARYLSILANES WITH MISCELLANEOUS ELECTROPHILES

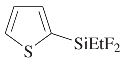
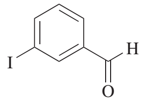
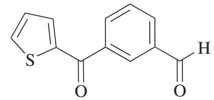
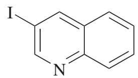
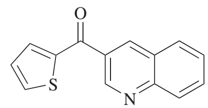
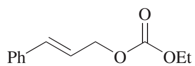
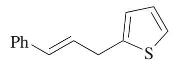
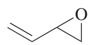
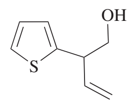
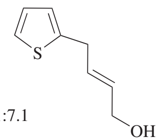
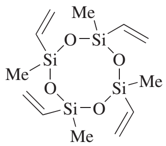
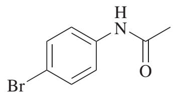
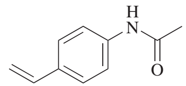
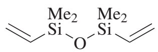
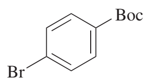
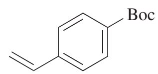
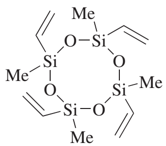
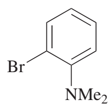
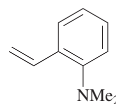
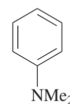
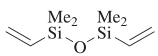
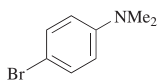
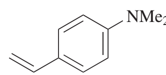
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 150%		$[allylPdCl]_2$ (2.5%), KF (150%), CO (1 atm), DMI, 100°, 6 h	 (72)	179, 182
150%		$[allylPdCl]_2$ (2.5%), KF (150%), CO (1 atm), DMI, 100°, 19 h	 (78)	179, 182
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), Ph_3P (5%), benzene, 60°, 19 h	 (97)	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), Ph_3P (5%), benzene, 60°	 +  (60) 1:7.1	175

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 12 h	 (77)	318
 130%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (300%), DMF, 40°, 2 h	 (60)	262
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 24 h	 (78) +  (10)	318
 200%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (400%), DMF, 40°, 24 h	 (70)	262

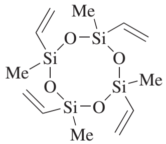
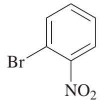
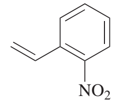
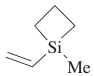
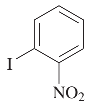
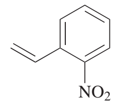
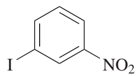
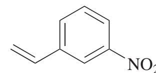
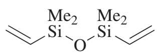
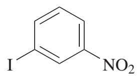
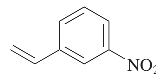
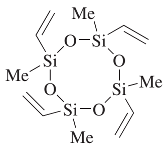
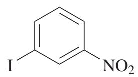
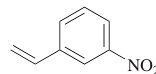
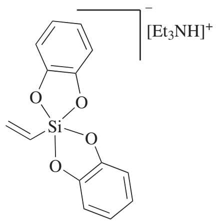
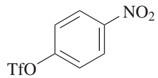
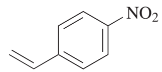
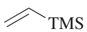
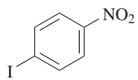
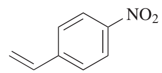
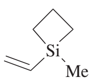
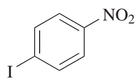
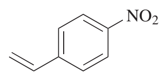
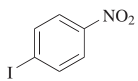
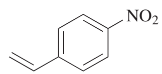
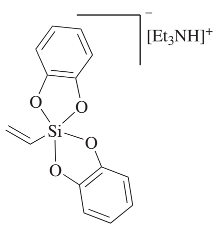
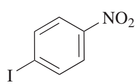
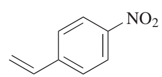
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 2 h		(85)	318
 120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1.5 h		(86)	40
120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h		(92)	40
 75%		$Pd(dba)_2$ (2.5%), $Ph_3P(O)$ (2.5%), KOTMS (350%), DMF, rt, 1 h		(76)	262
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(87)	267

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$Pd(PPh_3)_4$ (5%), LiCl (300%), dioxane, reflux, 12 h	 (57)	22
		$[allylPdCl]_2$ (2.5%), TASF (130%), HMPA, 50°	 (83)	23
 120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h	 (90)	40
 50%		Catechol (50%), $[allylPdCl]_2$ (5%), $(EtO)_3P$ (10%), Et_3N (50%), dioxane, reflux, 30 h	 (86)	87
		$PdCl_2(PhCN)_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 60 h	 (80)	22

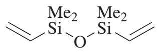
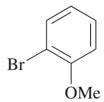
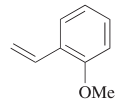
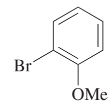
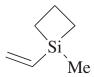
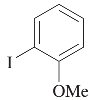
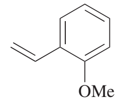
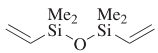
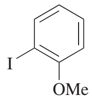
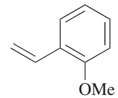
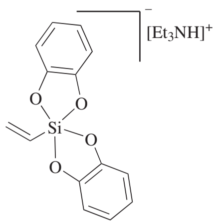
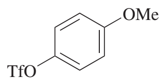
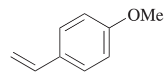
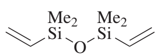
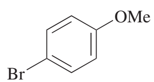
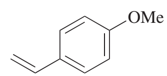
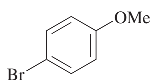
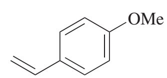
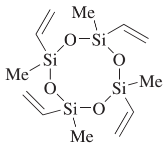
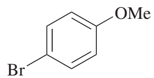
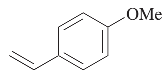
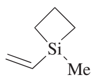
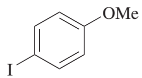
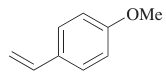
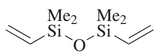
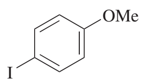
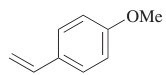
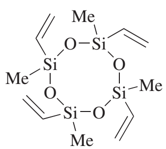
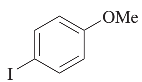
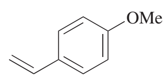
 200%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (400%), DMF, 40°, 24 h	 (72) +  (15)	262
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 10 h	 (75)	40
 75%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), DMF, rt, 14 h	 (68)	262
		$Pd(PPh_3)_4$ (5%), LiCl (300%), dioxane, reflux, 60 h	 (52)	22
 200%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (400%), DMF, 35°, 4 h	 (74)	262
110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 1 h	 (71)	262

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 10 h	 (86)	318
 150%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (450%), THF, rt, 4 h	 (74)	40
 75%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), DMF, rt, 1.5 h	 (80)	262
 150%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 240 min	 (46)	267

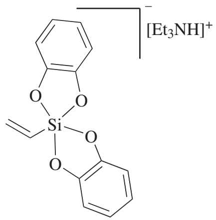
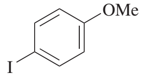
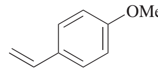
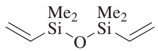
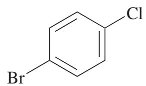
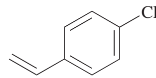
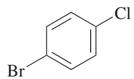
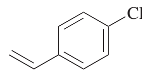
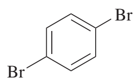
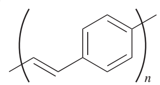
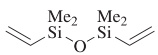
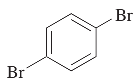
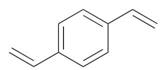
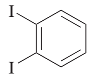
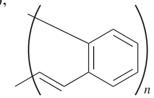
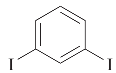
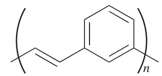
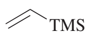
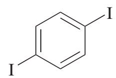
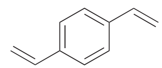
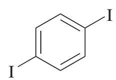
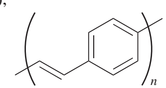
		$PdCl_2PhCN_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 110 h		(47)	22
 110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h		(55)	262
130%		JohnPhos (5%), $KOSiEt_3$ (300%), $[allylPdCl]_2$ (2.5%), DMF, 40°, 3 h		(50)	262
		1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), CuCl (2%), dioxane, 110° 2. Electrophile (90%), $Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h		(92)	104
 260%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (600%), DMF, 40°, 2 h		(48)	262

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
		1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), $CuCl$ (2%), dioxane, 110° 2. Electrophile (90%), Pd_2dba_3 (1%), TBAF (240%), dioxane, 80°, 24 h		(90)	104
		1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), $CuCl$ (2%), dioxane, 110° 2. Electrophile (90%), Pd_2dba_3 (1%), TBAF (240%), dioxane, 80°, 24 h		(90)	104
 220%		$[allylPdCl]_2$ (2.5%), TASF (220%), HMPA, 50°		(84)	23
		1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), $CuCl$ (2%), dioxane, 110° 2. Electrophile (90%), $Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 16 h		(98)	104

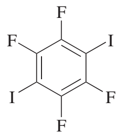
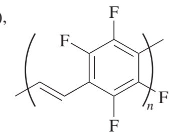
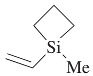
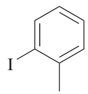
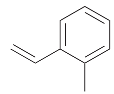
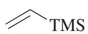
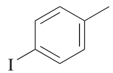
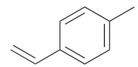
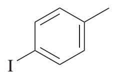
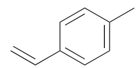
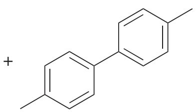
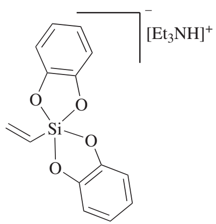
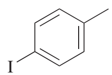
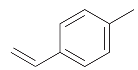
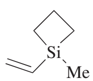
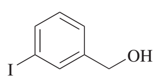
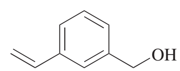
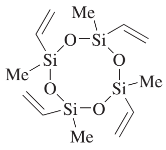
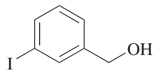
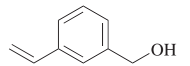
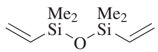
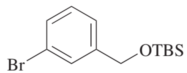
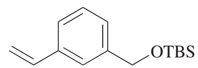
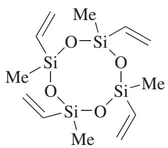
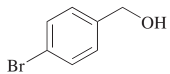
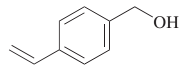
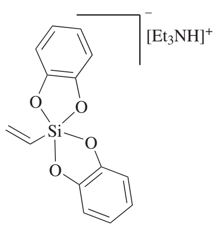
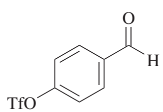
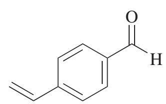
		1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), $CuCl$ (2%), dioxane, 110° 2. Electrophile (90%), Pd_2dba_3 (1%), TBAF (240%), dioxane, 80°, 48 h		(43)	104
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 16 h		(70)	40
 130%		$[allylPdCl]_2$ (2.5%), TASF (130%), HMPA, 50°		(89)	23
		TBAF, $Pd(dba)_2$ (cat.) DMF, 85°	 (66) + 	(18)	70
		$PdCl_2(PhCN)_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 60 h		(38)	22
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 7.5 h		(79)	40

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
 120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 480 min		(59)	267
 200%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (400%), THF, 40°, 24 h		(64)	262
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 14 h		(54)	318
		$Pd(PPh_3)_4$ (5%), LiCl (300%), dioxane, reflux, 60 h		(41)	22

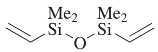
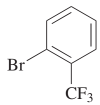
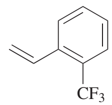
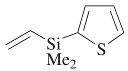
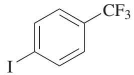
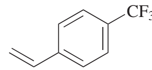
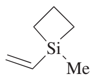
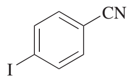
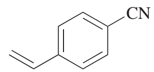
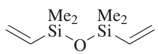
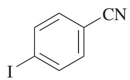
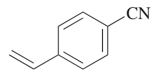
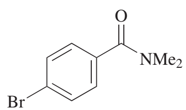
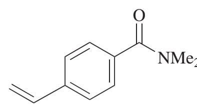
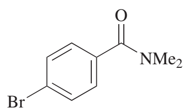
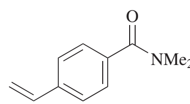
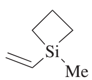
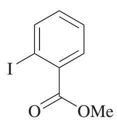
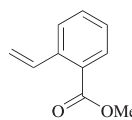
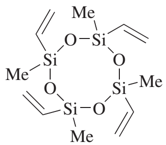
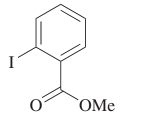
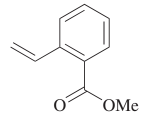
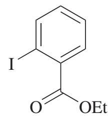
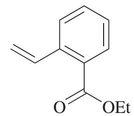
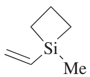
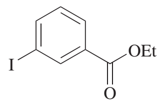
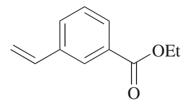
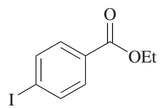
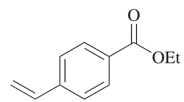
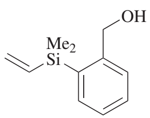
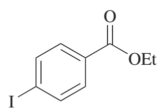
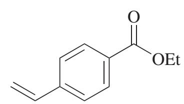
 110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h		(52)	262
 120%		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 0.5 h		(90)	49
 120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h		(87)	40
 75%		$Pd(dba)_2$ (2.5%), $Ph_3P(O)$ (2.5%), KOTMS (350%), DMF, rt, 0.5 h		(81)	262
130%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (300%), DMF, 40°, 2 h		(69)	262
110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h		(34)	262
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 14 h		(85)	40

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (200%), THF, rt, 480 min		(83)	267
50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 5 h		(86)	318
		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 1 h		(90)	40
120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h		(93)	40
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 35°, 19 h		(87)	150

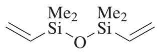
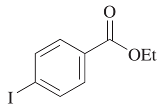
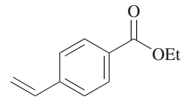
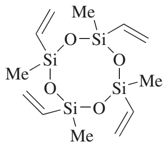
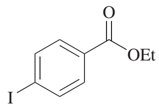
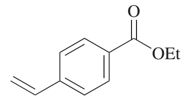
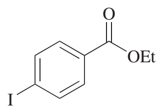
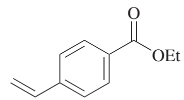
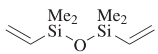
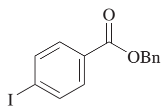
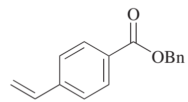
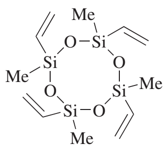
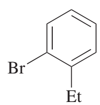
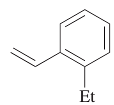
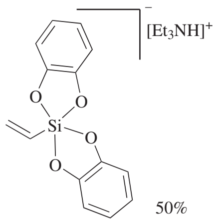
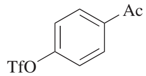
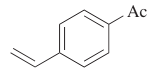
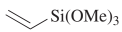
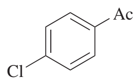
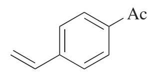
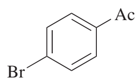
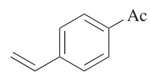
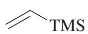
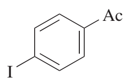
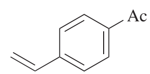
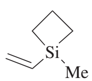
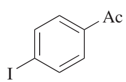
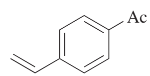
 75%		$Pd(dba)_2$ (2.5%), $Ph_3P(O)$ (2.5%), KOTMS (350%), DMF, rt, 0.5 h		(81)	262
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(85)	267
50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 5 h		(83)	318
 75%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), DMF, rt, 1.5 h		(74)	262
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 17 h		(75)	318

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 50%		$(Ph_3P)_4Pd$ (5%), LiCl (300%), dioxane, reflux, 110 h	 (68)	87
 200%		Pd cat. **5** (2%), NaOH (250%), TBAB (100%), H_2O, MW, 25 min	 (60)	257
200%		Pd cat. **5** (0.5%), NaOH (250%), TBAB (100%), H_2O, 120°, 20 h	 (89)	257
 130%		$[allylPdCl]_2$ (2.5%), TASF (130%), HMPA, 50°	 (86)	23
 120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h	 (85)	40

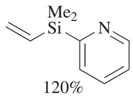
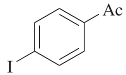
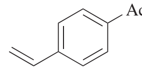
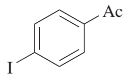
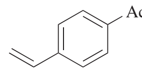
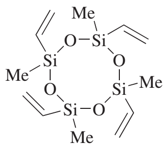
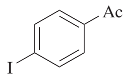
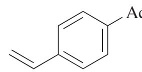
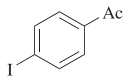
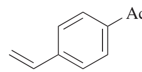
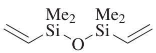
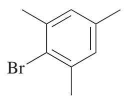
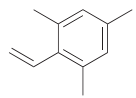
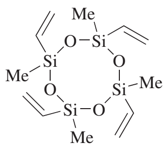
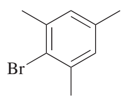
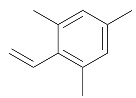
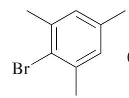
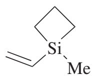
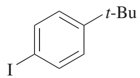
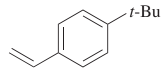
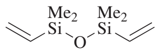
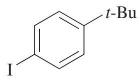
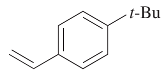
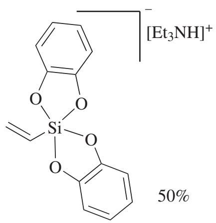
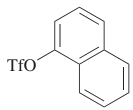
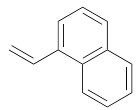
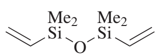
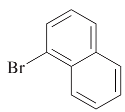
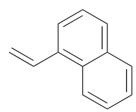
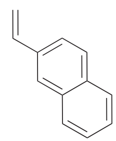
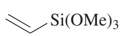
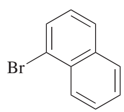
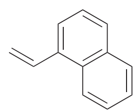
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (79)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (79)	169
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 3 h	 (91)	318
120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (88)	267
 200%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (400%), DMF, 40°, 24 h	 (99)	262
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 48 h	 (72) +  (5)	318

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 6 h	 (80)	40
 75%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), DMF, rt, 4 h	 (69)	262
 50%		$(Ph_3P)_4Pd$ (5%), LiCl (300%), dioxane, reflux, 30 h	 (59)	22, 87
 130%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (300%), DMF, rt, 12 h	 (80) +  (5)	262
 200%		Pd cat. **5** (1%), NaOH (250%), TBAB (100%), H_2O, 120°, 24 h	 (90)	257

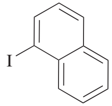
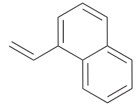
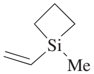
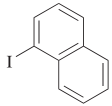
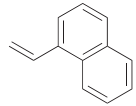
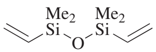
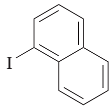
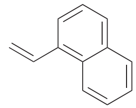
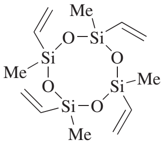
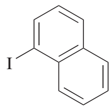
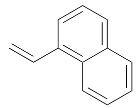
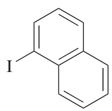
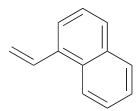
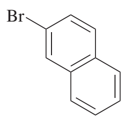
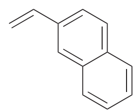
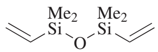
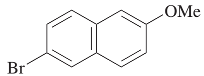
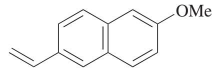
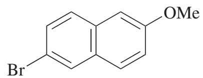
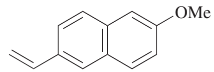
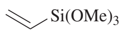
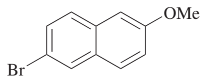
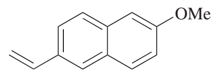
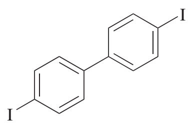
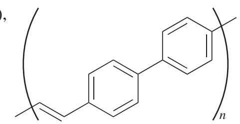
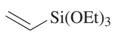
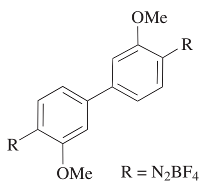
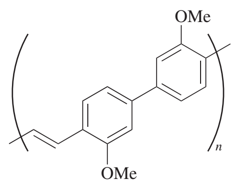
 130%		[allylPdCl]$_2$ (2.5%), TASF (130%), HMPA, 50°		(98)	23
 120%		Pd(dba)$_2$ (5%), TBAF (300%), THF, rt, 4 h		(86)	40
 75%		Pd(dba)$_2$ (5%), Ph$_3$P(O) (5%), KOTMS (350%), DMF, rt, 2.5 h		(80)	262
 50%		JohnPhos (10%), PdBr$_2$ (5%), TBAF (200%), THF, 50°, 3 h		(71)	318
120%		Pd(dba)$_2$ (5%), TBAF (200%), THF, rt, 3 h		(64)	267
50%		JohnPhos (10%), PdBr$_2$ (5%), TBAF (200%), THF, 50°, 3 h		(81)	318

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
 130%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (300%), DMF, rt, 4 h		(82)	262
110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h		(70)	262
 200%		Pd cat. **5** (0.5%), NaOH (250%), TBAB (100%), H_2O, MW, 10 min		(83)	257
	 90%	1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), CuCl (2%), dioxane, 110° 2. Electrophile, Pd_2dba_3 (1%), TBAF (240%), dioxane, 80°, 16 h		(98)	104
 120%	 R = N_2BF_4	$Pd(OAc)_2$ (10%), EtOH, 80°		(—)	256

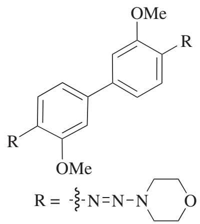
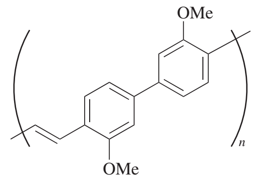
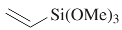
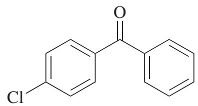
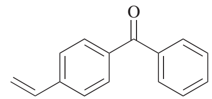
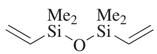
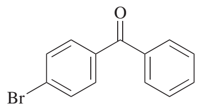
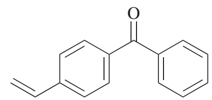
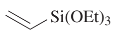
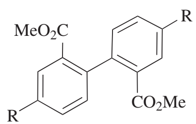
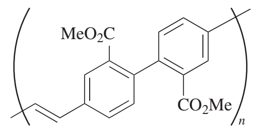
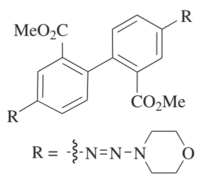
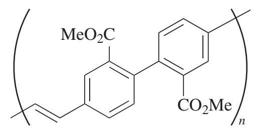
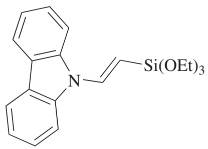
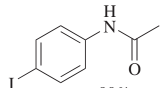
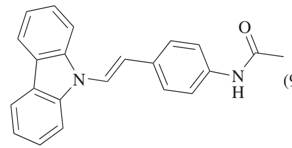
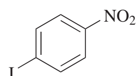
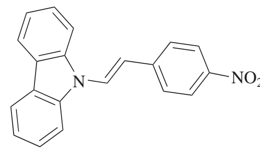
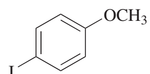
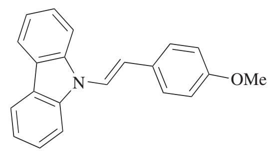
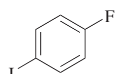
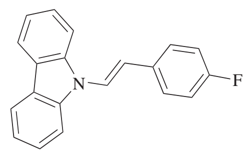
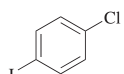
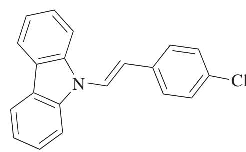
120%		$Pd(OAc)_2$ (10%), aq. $HClO_4$ (400%), EtOH, 80°		(—)	256
 200%		$Pd(OAc)_2$ (2%), NaOH (250%), TBAB (100%), H_2O, MW, 25 min		(61)	257
 120%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h		(93)	262
	 $R = N_2BF_4$	$Pd(OAc)_2$ (10%), EtOH, 80°		(—)	256
120%		$Pd(OAc)_2$ (10%), aq. $HClO_4$ (400%), EtOH, 80°		(—)	256

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 90%	$Pd_2(dba)_3$ (1%) TBAF (120%), THF, 30°, 48 h	 (91)	258
	 90%	$Pd_2(dba)_3$ (1%) TBAF (120%), THF, 30°, 24 h	 (98)	258
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 48 h	 (66)	258
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 48 h	 (79)	258
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 48 h	 (72)	258

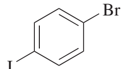
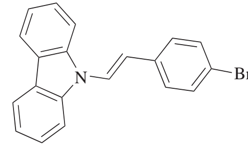
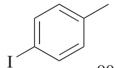
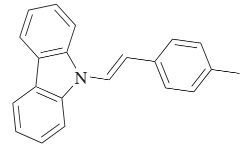
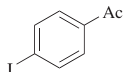
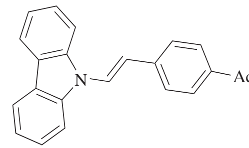
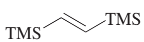
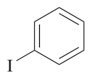
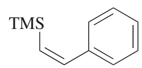
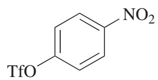
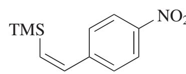
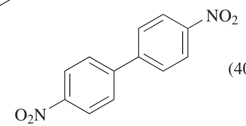
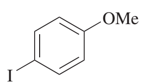
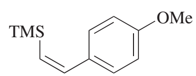
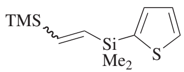
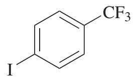
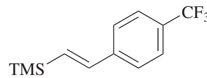
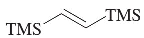
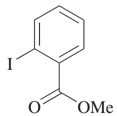
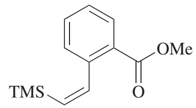
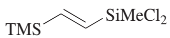
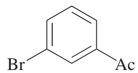
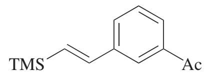
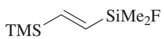
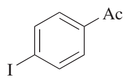
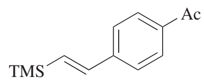
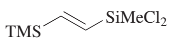
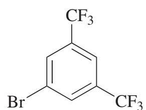
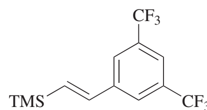
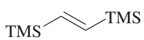
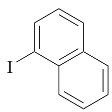
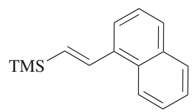
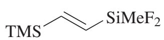
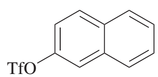
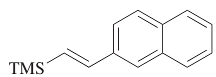
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 48 h	 (71)	258
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 48 h	 (81)	258
	 90%	$Pd_2(dba)_3$ (1%), TBAF (120%), THF, 30°, 24 h	 (86)	258
		$Pd(OAc)_2$ (3%), Et_3N (240%), DMF, 110°, 2 h	 (43)	101
		$Pd(OAc)_2$ (3%), Et_3N (240%), DMF, 110°, 2 h	 (25) +  (40)	101
		$Pd(OAc)_2$ (3%), Et_3N (240%), DMF, 110°, 2 h	 (57)	101

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
 120% (*E*)/(*Z*) = 96:4		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 1 h		(95) (*E*)/(*Z*) = 96:4	49
		$Pd(OAc)_2$ (3%), Et_3N (240%), DMF, 110°, 2 h		(49)	101
 120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 12 h		(62)	185
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 5.5 h		(67)	25
 120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 36 h		(74)	185
		$Pd(OAc)_2$ (3%), Et_3N (240%), DMF, 110°, 2 h		(55)	101
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 5 h		(74)	181

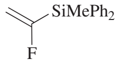
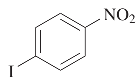
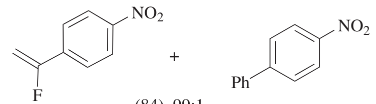
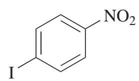
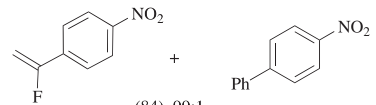
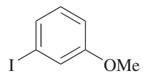
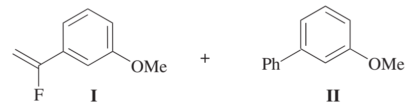
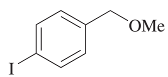
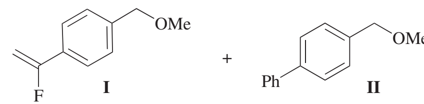
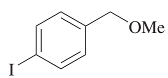
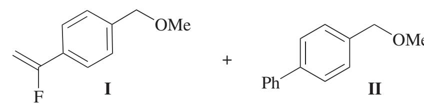
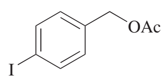
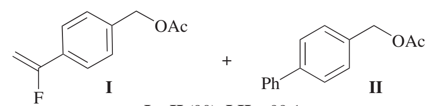
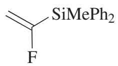
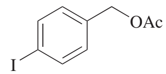
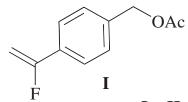
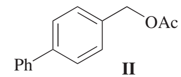
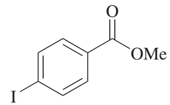
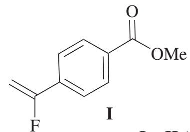
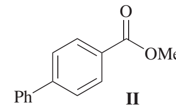
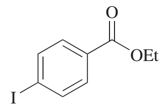
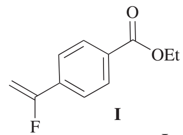
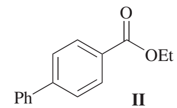
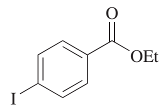
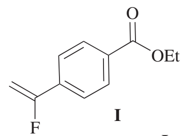
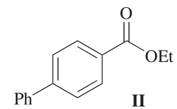
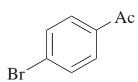
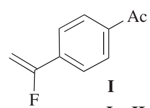
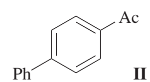
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 (84) 99:1	163, 164
		$(Ph_3P)_4Pd$ (5%), CsF (230%), CuI (5%), DMI/THF, 9:1, rt	 (84) 99:1	164
150%		$(Ph_3P)_4Pd$ (5%), CuI (5%), CsF (230%), DMI, 50°	 **I** + **II** (63), **I**:**II** = 93:7	164
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 **I** + **II** (86), **I**:**II** = 98:2	163, 164
		$(Ph_3P)_4Pd$ (5%), CsF (230%), CuI (5%), DMI, rt	 **I** + **II** (86), **I**:**II** = 98:2	164
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 **I** + **II** (90), **I**:**II** = 99:1	163, 164

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 150%		$(Ph_3P)_4Pd$ (5%), CsF (230%), CuI (5%), DMI, rt	 **I** +  **II** **I** + **II** (90), **I**:**II** = 99:1	164
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 **I** +  **II** **I** + **II** (89), **I**:**II** = 98:2	163, 164
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 **I** +  **II** **I** + **II** (91), **I**:**II** = 99:1	163, 164
		$(Ph_3P)_4Pd$ (5%), CsF (230%), CuI (5%), DMI, rt	 **I** +  **II** **I** + **II** (91), **I**:**II** = 99:1	164
		$(Ph_3P)_4Pd$ (5%), CsF (1.5%), CuI (5%), DMI, rt	 **I** +  **II** **I** + **II** (62), **I**:**II** = 84:16	163

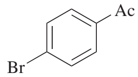
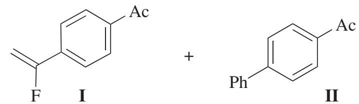
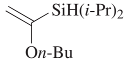
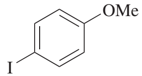
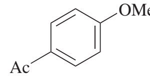
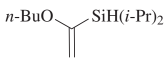
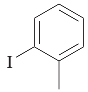
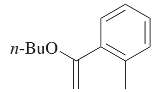
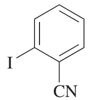
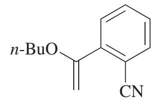
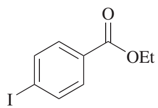
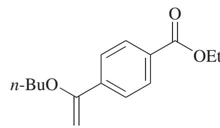
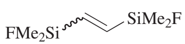
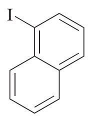
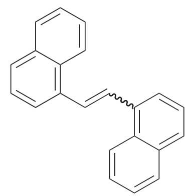
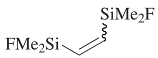
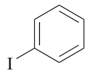
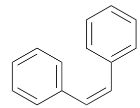
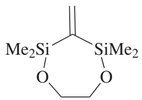
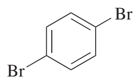
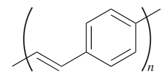
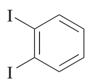
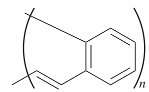
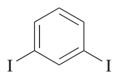
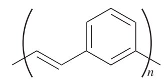
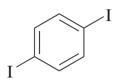
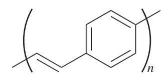
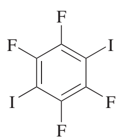
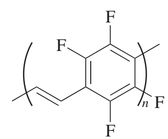
150%		$(Ph_3P)_4Pd$ (5%), CsF (230%), CuI (10%), DMI, rt	 I + II (62), I:II = 84:16		164
 140%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%) 3. 1 N HCl, 10 min		(94)	171
 140%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), 30 min		(83)	171
140%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), 15 h		(76)	171
140%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), 10 min		(89)	171
 (*E*)/(*Z*) = 9:1	 200%	$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 24 h		(45) (*E*)/(*Z*) = 9:1	25

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
 (*E*)/(*Z*) = 1:4	 200%	$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 24 h	 (43) (*E*)/(*Z*) = 1:4	25
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h	 (94)	104
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h	 (97)	104
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h	 (98)	104
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 16 h	 (96)	104
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 48 h	 (35)	104

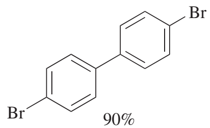
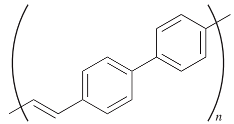
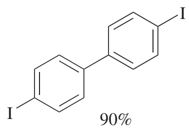
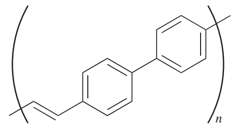
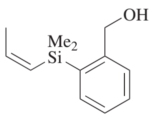
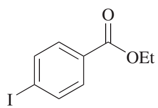
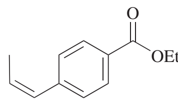
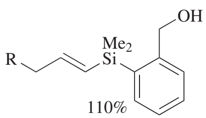
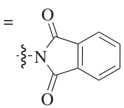
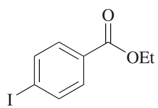
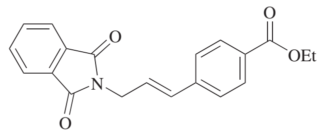
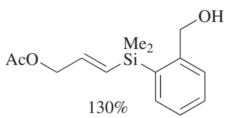
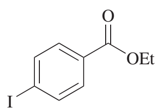
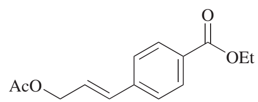
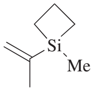
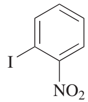
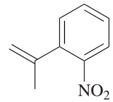
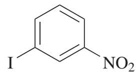
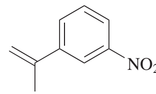
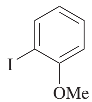
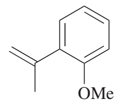
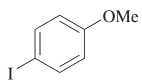
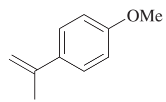
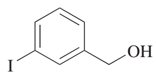
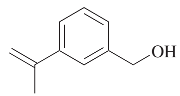
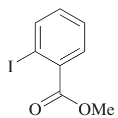
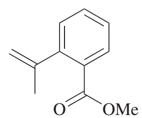
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h		(98)	104
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h		(98)	104
C_3					
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 19 h		(91) (*Z*)/(*E*) = 94:6	150, 151
 110% R = 		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 24 h		(93)	150
 130%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 25 h		(93)	150

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_3					
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 4 h		(79)	40
120%		$Pd(dba)_2$ (1%), TBAF (200%), THF, rt, 1 h		(84)	40
120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 1 h		(73)	40
120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min		(85)	40
120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min		(87)	40
120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (300%), THF, rt, 20 h		(78)	40

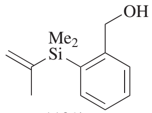
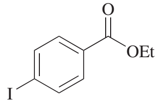
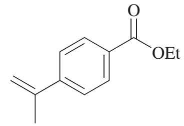
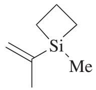
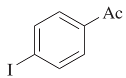
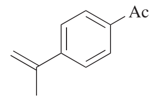
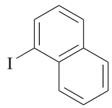
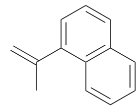
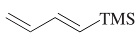
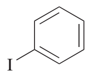
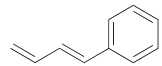
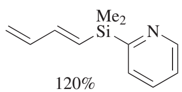
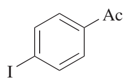
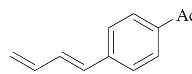
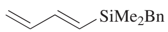
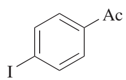
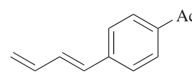
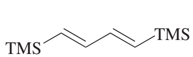
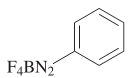
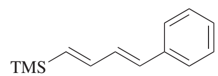
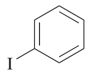
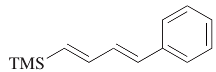
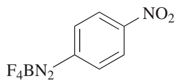
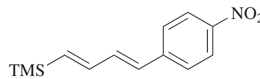
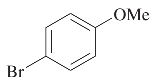
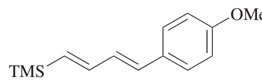
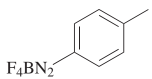
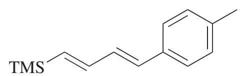
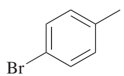
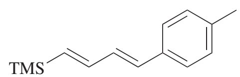
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 24 h		(96)	150, 151
 120%		Pd(dba)$_2$ (1%), TBAF (200%), THF, rt, 60 min		(89)	40
120%		Pd(dba)$_2$ (5%), TBAF (300%), THF, rt, 10 min		(84)	40
C_4					
		[allylPdCl]$_2$ (2.5%), TBAF (110%), THF, 60°, 21 h		(75)	89
 120%		$PdCl_2$(PhCN)$_2$ (5%), TBAF (100%), THF, 60°		(75)	169
 120%		$PdCl_2$(PhCN)$_2$ (5%), TBAF (100%), THF, 60°		(75)	169
 120%		1. BCl_3, CH_2Cl_2, 0° 2. Pd(OAc)$_2$ (6%), dioxane, rt, 24 h		(45)	124

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_4					
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), NaOH (2 M), benzene, reflux		(98)	125
120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h		(40)	124
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), NaOH (2 M), benzene, reflux		(61)	125
120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h		(40)	125
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), NaOH (2 M), benzene, reflux		(73)	125

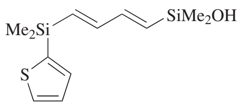
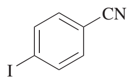
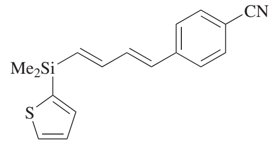
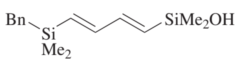
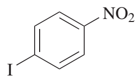
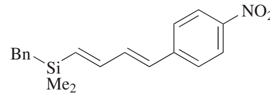
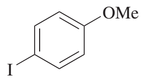
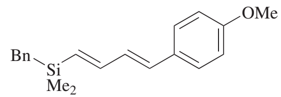
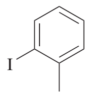
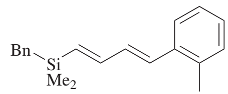
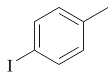
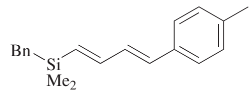
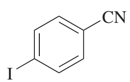
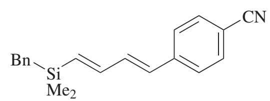
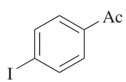
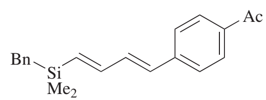
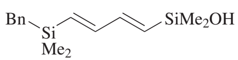
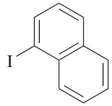
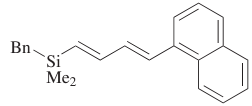
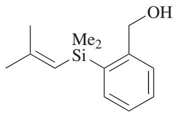
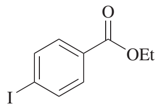
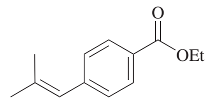
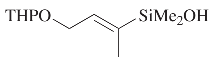
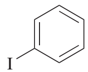
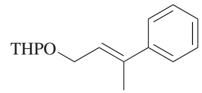
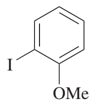
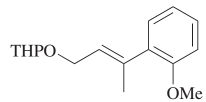
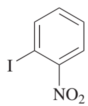
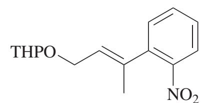
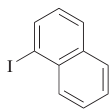
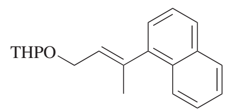
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 0.5 h		(83)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 0.5 h		(96)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 1 h		(88)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 6 h		(96)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 1 h		(85)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 0.5 h		(93)	44
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 18 h		(76)	44

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		$Pd(dba)_2$ (2.5%), KOTMS (200%), dioxane, rt, 4 h	 (91)	44
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 25 h	 (96) (*Z*)/(*E*) = 94:6	150, 151
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 40 min	 (91)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 100 min	 (77)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 115 min	 (76)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 200 min	 (90) (*E*)/(*Z*) = 93:7	79

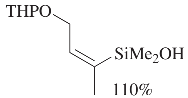
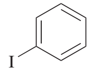
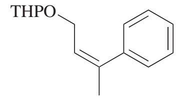
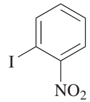
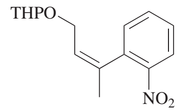
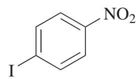
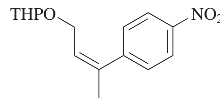
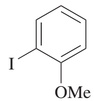
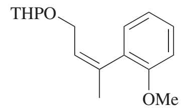
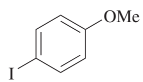
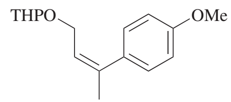
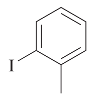
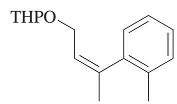
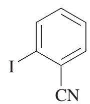
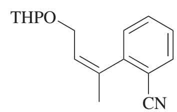
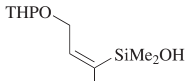
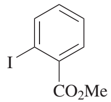
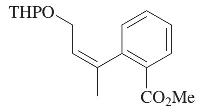
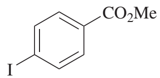
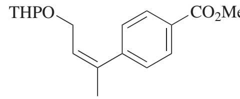
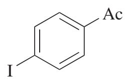
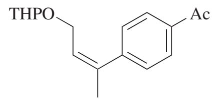
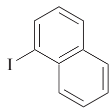
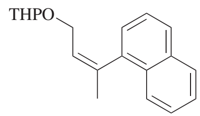
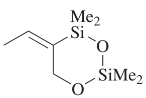
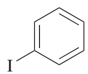
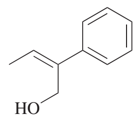
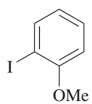
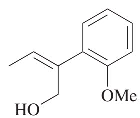
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 40 min		(75)	79
110%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (200%), THF, rt, 610 min		(77)	79
120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 400 min		(77)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 600 min		(70)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 390 min		(70)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 90 min		(79)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 580 min		(70)	79

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 120%		$Pd(dba)_2$ (5%), Ph_3As (10%), TBAF (200%), THF, 35°, 48 h	 (80)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, 35°, 150 min	 (82)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 40 min	 (73)	79
110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 140 min	 (76)	79
 105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 3.3 h; then 45°, 1.4 h	 (79)	264
105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 12.9 h; then 40°, 13 h	 (81)	264

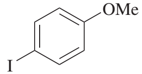
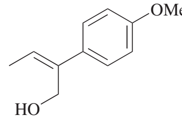
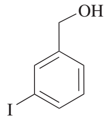
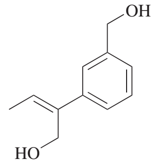
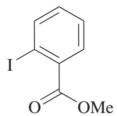
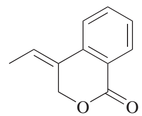
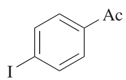
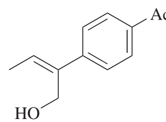
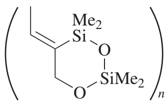
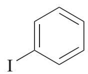
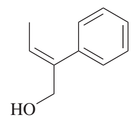
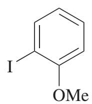
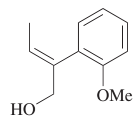
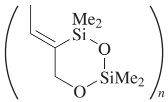
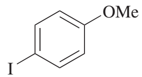
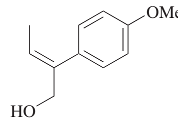
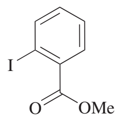
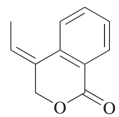
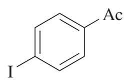
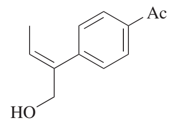
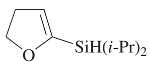
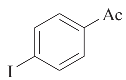
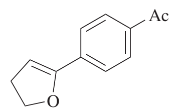
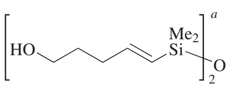
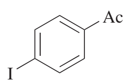
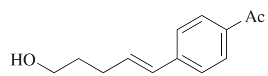
105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 3.2 h; then 35°, 2 h		(71)	264
105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 5.4 h; then 40°, 1.9 h		(81)	264
105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 16.3 h; then 40°, 24.5 h		(57)	264
105%		$Pd(dba)_2$ (5%), TBAF (200%), dioxane, rt, 10.1 h		(82)	264
 180%		$Pd(dba)_2$ (5%), TBAF (250%), dioxane, rt, 75 h		(57) (*E*)/(*Z*) = 97.7:2.3	264
180%		$Pd(dba)_2$ (5%), TBAF (250%), dioxane, rt, 67 h; then 40°, 10 h		(65) (*E*)/(*Z*) = 98.5:1.5	264

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 180%		$Pd(dba)_2$ (5%), TBAF (250%), dioxane, rt, 20 h; then 40°, 3.5 h	 (57) (*E*)/(*Z*) = 97.3:2.7	264
180%		$Pd(dba)_2$ (11%), TBAF (200%), dioxane, rt, 23 h; then 35°, 23 h	 (52)	264
180%		$Pd(dba)_2$ (5%), TBAF (250%), dioxane, rt, 22.5 h; then 40°, 10 h	 (64) (*E*)/(*Z*) = 98.5:1.5	264
 140%		1. TBAOH (300%) 2. $[allylPdCl]_2$ (2.5%), THF, rt, 10 min	 (71)	171
C_5				
 180%		1. t-$Bu_3Pt(DVDS)$ (cat.) $(SiHMe_2)_2O$ (90%), 30 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min	 (82)	261

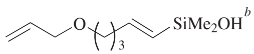
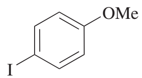
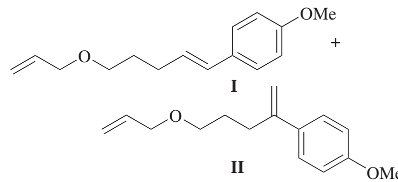
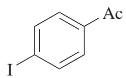
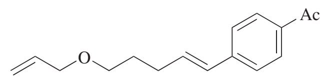
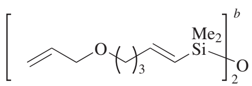
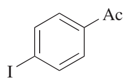
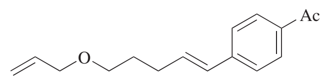
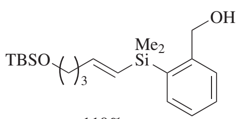
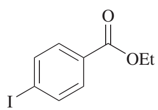
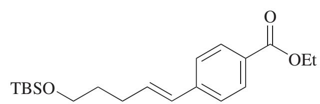
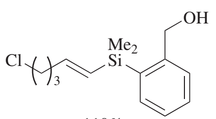
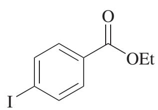
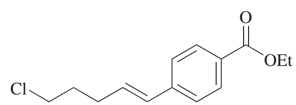
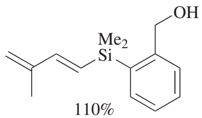
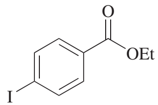
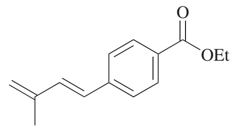
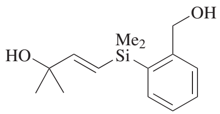
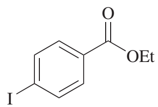
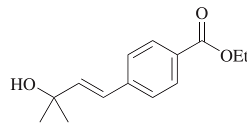
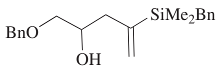
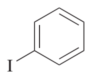
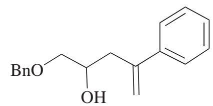
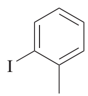
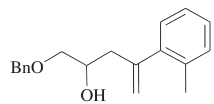
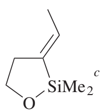
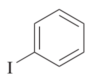
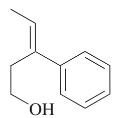
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 **I** + **II** (76), **I**:**II** = 99.6:0.4		261
		1. t-$Bu_3Pt(DVDS)$ (cat.), $(SiHMe_2)_2O$ (98%), 30 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(78)	261
		1. t-$Bu_3Pt(DVDS)$ (cat.), $(SiHMe_2)_2O$ (98%), 30 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(78)	261
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 31 h		(90)	150
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 50 h		(92)	150

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 25 h	 (93)	150
		$PdCl_2$ (5%), (2-furyl)$_3$P (10%), K_2CO_3 (220%), DMSO, 50°, 72 h	 (92)	150
	 150%	1. TBAF (220%), 10 min, THF, 0° 2. $Pd_2(dba)_3•CHCl_3$ (2.5%), rt, 4 h	 (95)	43
	 150%	1. TBAF (220%), 10 min, THF, 0° 2. $Pd_2(dba)_3•CHCl_3$ (2.5%), rt, 4 h	 (91)	43
 130%		TBAF (220%), $Pd(dba)_2$ (10%), THF, rt, 40 min	 (85) (*E*)/(*Z*) = 97.2:2.8	224

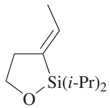
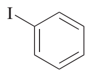
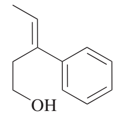
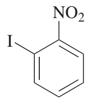
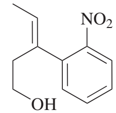
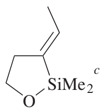
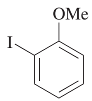
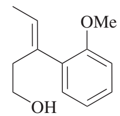
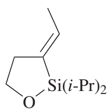
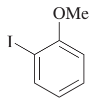
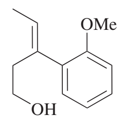
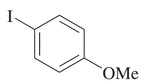
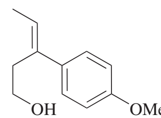
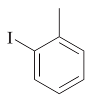
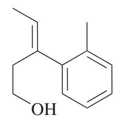
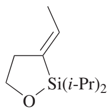
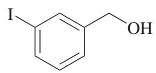
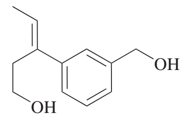
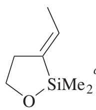
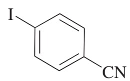
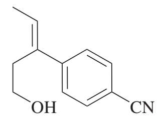
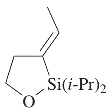
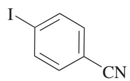
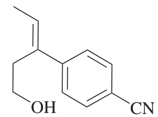
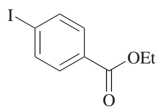
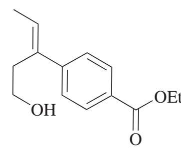
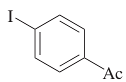
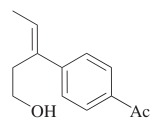
 110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, rt, 6.66 h		(88)	224
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 35°, 23 h		(56)	224
 130%		TBAF (220%), $Pd(dba)_2$ (10%), THF, 35°, 480 min		(75) (*E*)/(*Z*) = 98.3:1.7	224
 110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 35°, 10 h		(74)	224
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, rt, 6.5 h		(72)	224
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, rt, 6.83 h		(74)	224

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
 110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, rt, 6 h	 (81)	224
 [c] 130%		TBAF (220%), $Pd(dba)_2$ (10%), THF, rt, 40 min	 (74) (*E*)/(*Z*) = 96.7:3.3	224
 110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 45°, 46 h	 (70)	224
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 45°, 16 h	 (86)	224
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, rt, 6 h	 (70)	224

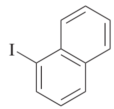
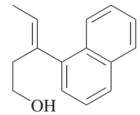
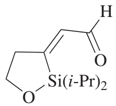
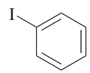
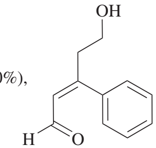
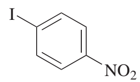
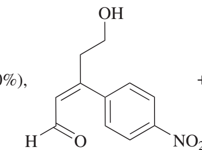
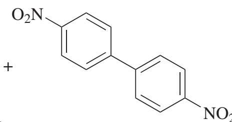
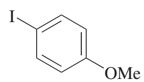
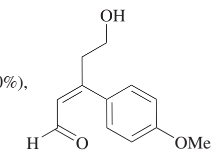
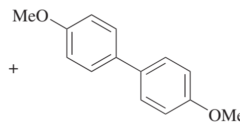
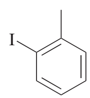
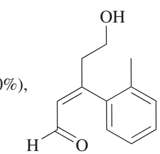
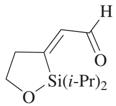
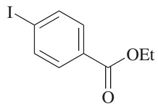
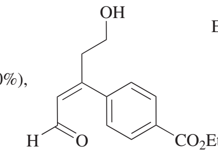
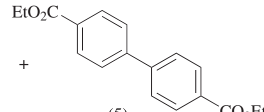
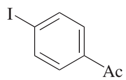
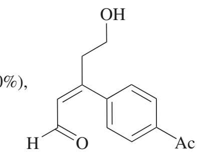
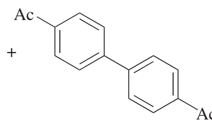
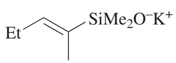
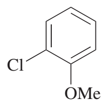
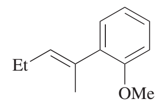
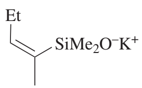
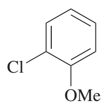
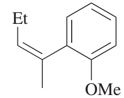
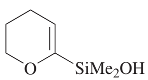
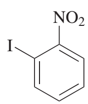
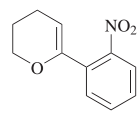
110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 35°, 8 h	 (76) $(E)/(Z) = 96.2:3.8$	224
 130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 2 h	 (93)	81
130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 1 h	 (83) +  (13)	81
130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 2 h	 (87) +  (5)	81
150%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (400%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 4 h	 (79)	81

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
 130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 2 h	 (92) +  (5)	81
130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 2 h	 (91) +  (7)	81
 150% (*E*)/(*Z*) = 98.9:1.1		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 66°, 0.5 h	 (97) (*E*)/(*Z*) = 98.8:1.2	80
 150% (*Z*)/(*E*) = 98.5:1.5		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 66°, 0.5 h	 (89) (*Z*)/(*E*) = 98.6:1.4	80
 120%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), rt, THF, 10 min	 (85)	171

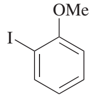
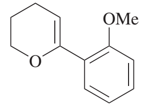
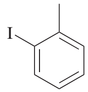
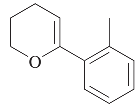
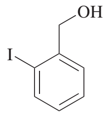
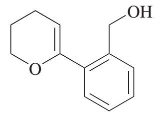
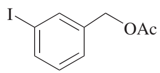
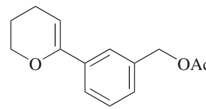
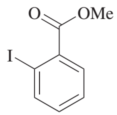
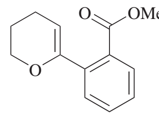
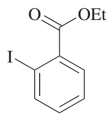
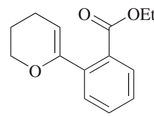
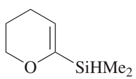
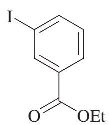
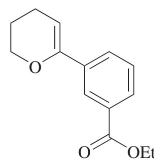
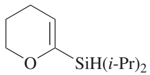
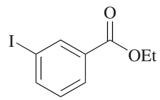
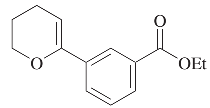
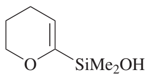
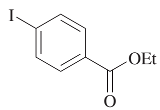
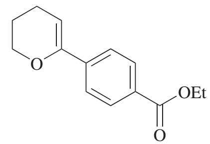
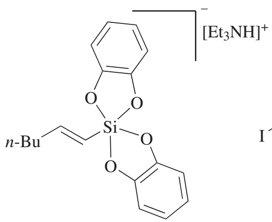
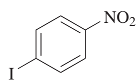
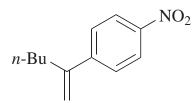
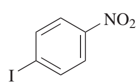
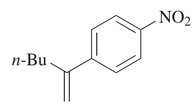
120%		1. TBAF (200%) 2. [allylPdCl]$_2$ (2.5%), rt, THF, 10 min		(74)	171
120%		1. TBAF (200%) 2. Pd(dba)$_2$ (5%), rt, THF, 20 min		(80)	171
120%		1. TBAF (200%) 2. Pd(dba)$_2$ (5%), rt, THF, 20 min		(88)	171
120%		1. TBAF (200%) 2. [allylPdCl]$_2$ (2.5%), rt, THF, 20 min		(87)	171
120%		1. TBAF (200%) 2. [allylPdCl]$_2$ (2.5%), rt, THF, 4 h		(92)	171
120%		1. TBAF (200%) 2. [allylPdCl]$_2$ (2.5%), rt, THF, 10 min		(86)	171
		1. TBAF (200%) 2. [allylPdCl]$_2$ (2.5%), rt, THF, 10 min		(81)	171

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5					
 120%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), rt, THF, 10 min		(81)	171
 120%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), rt, THF, 10 min		(86)	171
C_6					
		$[allylPdCl]_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 110 h		(64)	87
		$PdCl_2(PhCN)_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 40 h		(54)	22

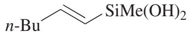
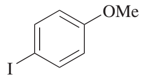
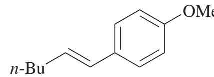
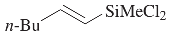
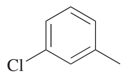
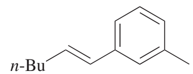
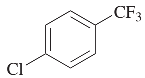
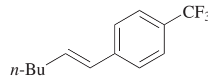
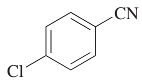
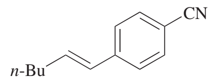
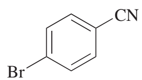
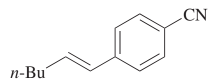
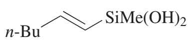
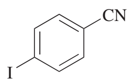
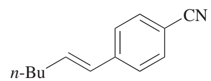
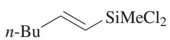
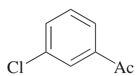
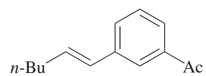
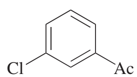
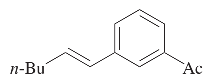
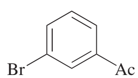
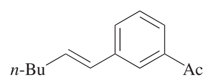
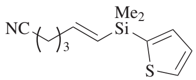
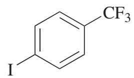
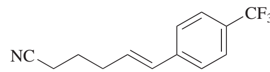
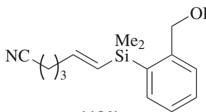
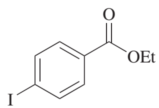
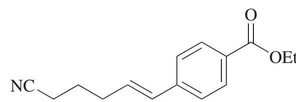
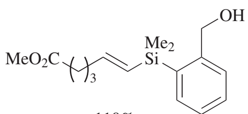
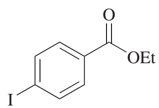
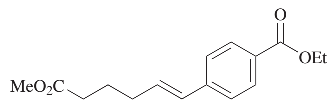
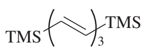
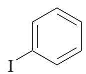
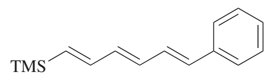
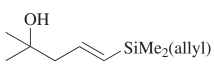
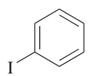
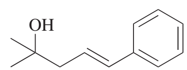
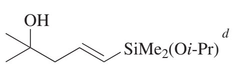
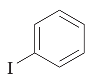
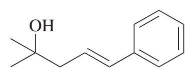
 120%		$(Ph_3P)_4P$ (5%), Ag_2O (100%), THF, 60°, 4 h		(79)	37
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (2.5%), NaOH (600%), C_6H_6, 80°, 12 h		(91)	185
120%		$(i\text{-}Pr_3P)_2PdCl_2$ (2.5%), NaOH (600%), C_6H_6, 80°, 12 h		(95)	185
120%		$(Et_3P)_2PdCl_2$ (0.5%), TBAF (300%), THF, 90°, 20 h		(83)	187
120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 12 h		(80)	185
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 4 h		(87)	37
 120%		$(Et_3P)_2PdCl_2$ (0.5%), TBAF (300%), THF, 90°, 20 h		(83)	187
120%		$(i\text{-}Pr_3P)_2PdCl_2$ (2.5%), NaOH (600%), C_6H_6, 80°, 12 h		(65)	185
120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 5 h		(79)	185

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 120% (*E*)/(*Z*) = 75:25		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 1 h	 (90) (*E*)/(*Z*) = 81:19	49
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 19 h	 (95)	150, 151
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 18 h	 (92)	150
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), NaOH (2 M), benzene, reflux	 (45)	90, 125
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile	 (85)	157
		$Pd_2(dba)_3$ (cat.), TBAF, THF, rt	 (71)	222

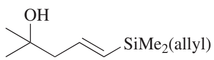
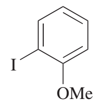
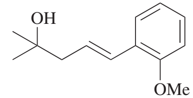
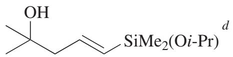
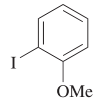
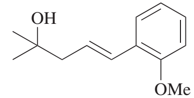
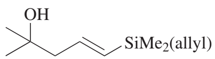
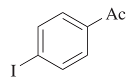
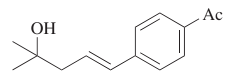
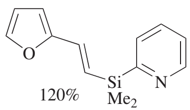
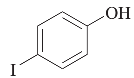
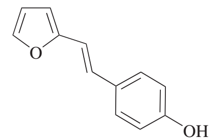
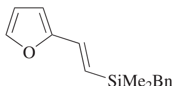
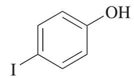
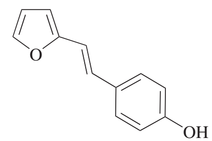
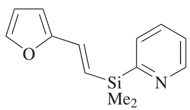
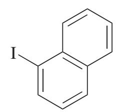
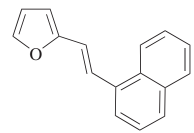
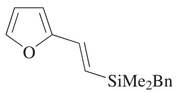
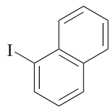
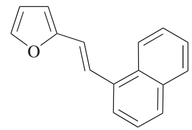
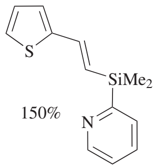
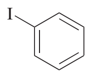
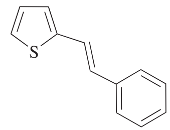
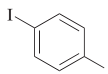
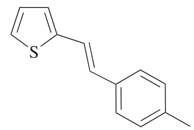
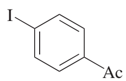
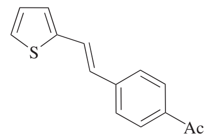
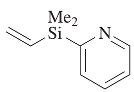
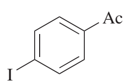
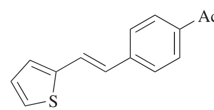
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(65)	157
		$[allylPdCl]_2$ (cat.), TBAF, THF, rt		(45)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(87)	157
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(73)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(73)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(98)	169

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(98)	169
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(90)	170
150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(93)	170
150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(90)	170
 150%		1. 2-Iodothiophene (130%), $Pd(OAc)_2$ (10%), $(2\text{-furyl})_3P$ (10%), Et_3N (160%), THF, 60° 2. Electrophile, TBAF (230%)		(93)	170

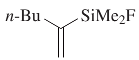
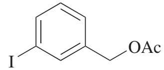
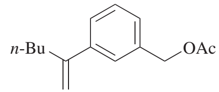
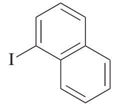
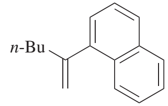
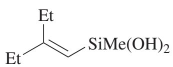
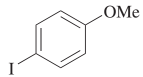
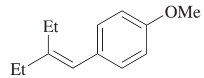
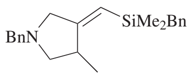
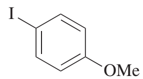
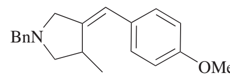
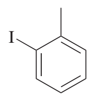
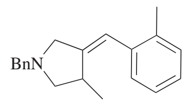
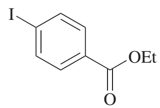
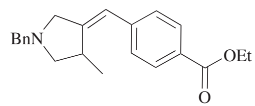
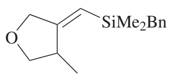
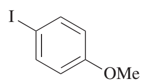
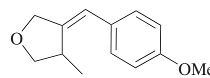
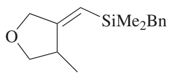
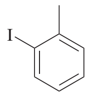
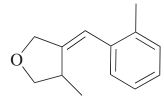
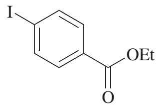
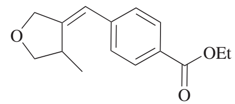
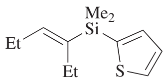
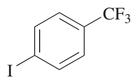
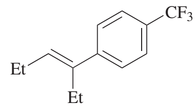
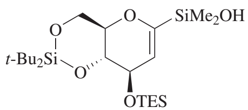
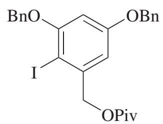
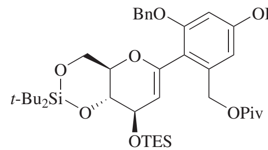
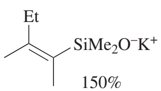
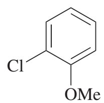
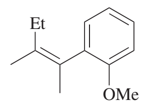
		[allylPdCl]$_2$ (2.5%), TBAF (150%), THF, 22 h		(83)	25
		[allylPdCl]$_2$ (2.5%), TBAF (150%), THF, 22 h		(74)	25
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 18 h		(99)	37
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt		(90)	45
110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt		(85)	45
110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt		(72)	45
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt		(89)	45

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt	 (77)	45
110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt	 (88)	45
 120%		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 1 h	 (86)	49
		$Pd_2(dba)_3$•$CHCl_3$ (5%), *t*-BuONa (200%), toluene, 50°, 5 h	 (82)	215
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 66°, 0.75 h	 (95) (*Z*)/(*E*) > 99:1	80

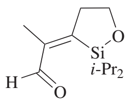
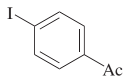
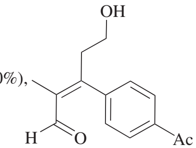
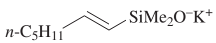
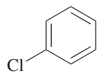
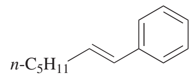
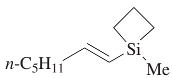
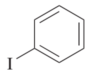
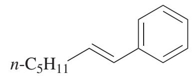
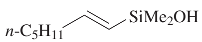
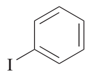
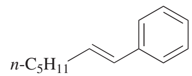
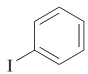
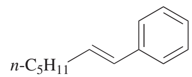
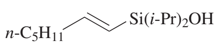
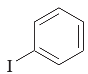
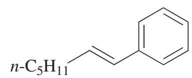
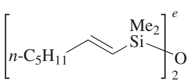
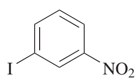
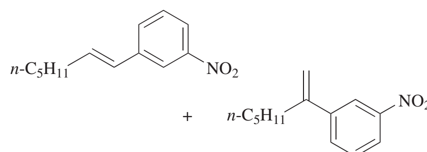
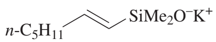
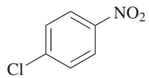
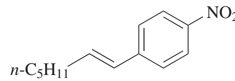
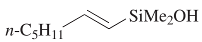
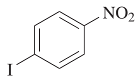
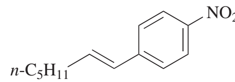
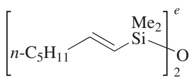
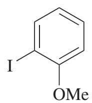
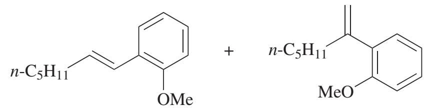
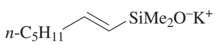
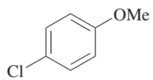
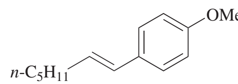
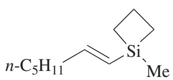
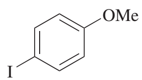
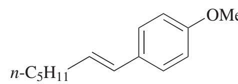
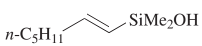
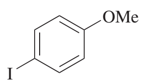
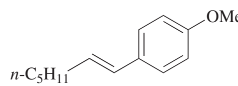
	Silane	Aryl halide	Conditions	Product(s) and Yield(s) (%)	Refs.
	 130%		$[allylPdCl]_2$ (10%), CuI (20%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (5%), DMF, rt, 7 h	 (83)	81
C_7					
	 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1.5 h	 (93) (*E*)/(*Z*) = 99.4:0.6	80
	 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 (91) (*E*)/(*Z*) = 99.9:0.1	38
	 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (91) (*E*)/(*Z*) = 97.8:2.2	31
			$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 0.5 h	 (91) (*E*)/(*Z*) = 99.3:0.7	32
	 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (82) (*E*)/(*Z*) = 99.2:0.8	31
	 130%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (85) (*E*)/(*Z* + *cine*) = 97.5:2.5	261

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 0.33 h	 (87) (*E*)/(*Z*) = 99.2:0.8	80
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 0.25 h	 (95) (*E*)/(*Z*) = 98.5:1.5	32
 [e] 130%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (82) (*E*)/(*Z* + *cine*) = 99.4:0.6	261
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 66°, 3.5 h	 (89) (*E*)/(*Z*) = 99.6:0.4	80
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 (94) (*E*)/(*Z*) = 99:1	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (95) (*E*)/(*Z*) = 97.2:2.8	31

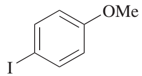
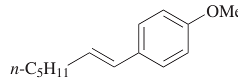
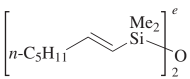
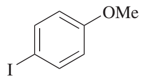
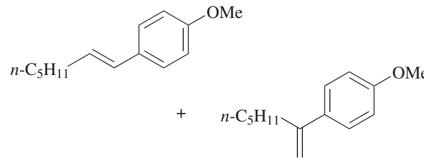
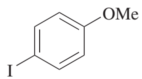
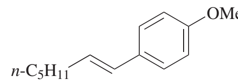
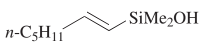
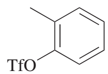
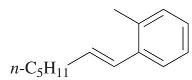
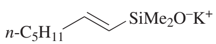
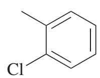
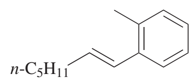
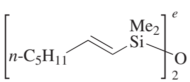
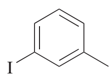
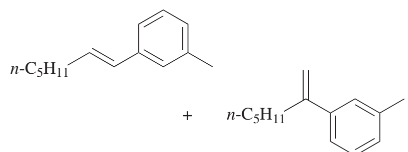
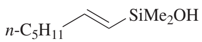
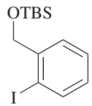
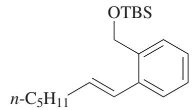
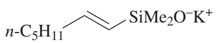
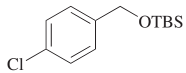
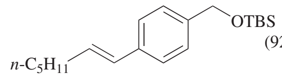
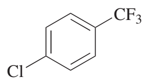
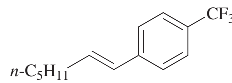
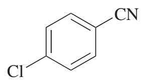
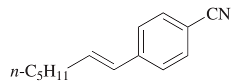
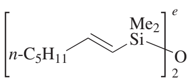
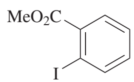
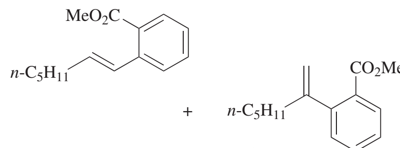
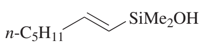
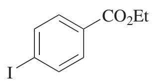
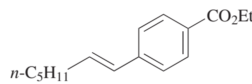
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 1 h	 (88) (*E*)/(*Z*) = 99.3:0.7	32
 130%		1. *t*-Bu_3Pt(DVDS) (cat.), $(SiHMe_2)_2O$ (130–200%), 30 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (84) (*E*)/(*Z*)/*cine* = 96.5:1.4:2.1	261
130%		1. *t*-Bu_3Pt(DVDS) (cat.), $(SiHMe_2)_2O$, 60 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min	 (83)	319
 110%		JohnPhos (10%), $PdBr_2$ (5%), TBAF•$6H_2O$ (200%), dioxane, rt, 16 h	 (85) (*E*)/(*Z*) = >99.9:0.1	202
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 2 h	 (95) (*E*)/(*Z*) = 99.8:0.2	162
 130%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (78) (*E*)/(*Z* + *cine*) = 97.4:2.6	80, 261

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 9 h	 (80) (*E*)/(*Z*) = 99.5:0.5	32
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1.5 h	 (92) (*E*)/(*Z*) = 98.8:1.2	80
150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1 h	 (91) (*E*)/(*Z*) = 99.7:0.3	80
150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 2 h	 (91) (*E*)/(*Z*) = 99.2:0.8	80
 130%		$Pd(dba)_2$ (5%), PhAs (10%), TBAF (200%), THF, rt, 20 h	 (88) (*E*)/(*Z* + *cine*) = 96.7:3.3	261
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 0.25 h	 (85) (*E*)/(*Z*) = 99.8:0.2	32

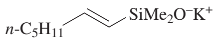
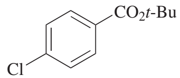
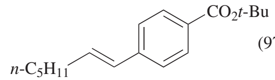
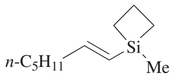
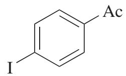
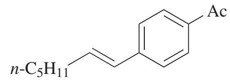
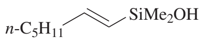
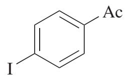
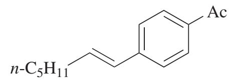
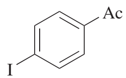
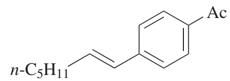
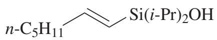
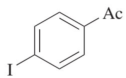
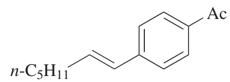
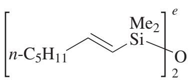
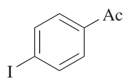
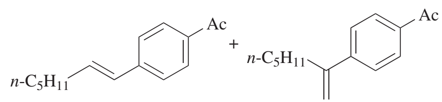
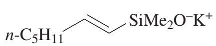
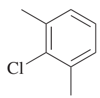
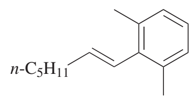
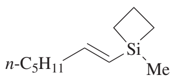
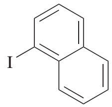
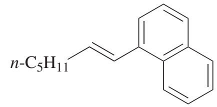
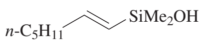
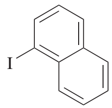
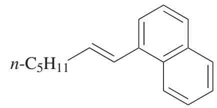
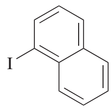
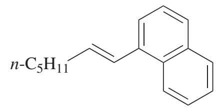
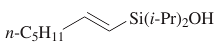
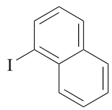
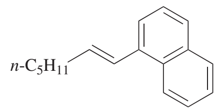
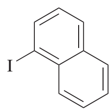
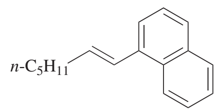
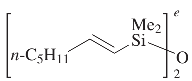
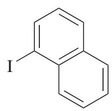
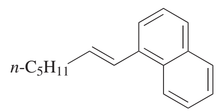
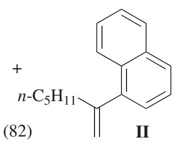
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 0.5 h	 (97) (*E*)/(*Z*) = 99.6:0.4	80
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 (84) (*E*)/(*Z*) = 99.7:0.3	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (93) (*E*)/(*Z*) = 96.5:3.5	31
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 9 h	 (82) (*E*)/(*Z*) = 98.8:1.2	32
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (80) (*E*)/(*Z*) = 99.5:0.5	31
 130%		1. t-$Bu_3Pt(DVDS)$ (cat.), $(SiHMe_2)_2O$ (130–200%), 30 min 2. $Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 **I** **I + II** (94) **II** (*E*)/(*Z*)/*cine* = 99.1:0.4:0.5	261
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 2 h	 (95) (*E*)/(*Z*) = 99.7:0.3	80

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 30 min	 (93) (*E*)/(*Z*) = 99.8:0.2	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min	 (89) (*E*)/(*Z*) = 96.5:3.5	31
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 2 h	 (93) (*E*)/(*Z*) = 97.9:2.1	32
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min	 (85) (*E*)/(*Z*) = 98.4:1.6	31
110%		$Pd(dba)_2$ (5%), TBAOH (200%), THF, rt, 30 min	 (78) (*E*)/(*Z*) = 99.2:0.8	31
 130%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 **I** +  **II** **I** + **II** (82) (*E*)/(*Z*)/*cine* = 98.4:0.1:1.5	261

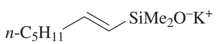
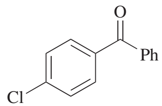
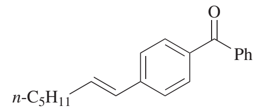
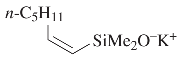
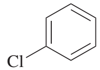
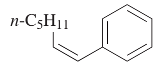
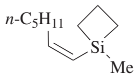
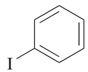
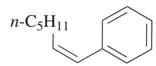
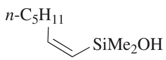
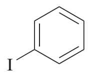
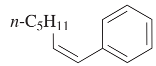
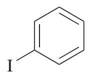
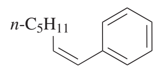
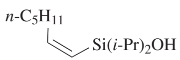
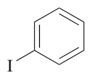
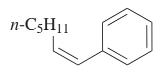
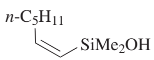
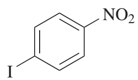
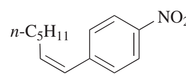
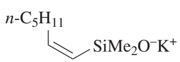
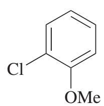
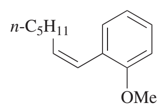
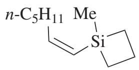
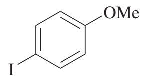
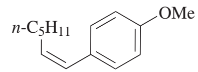
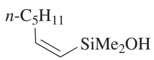
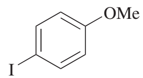
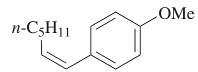
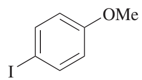
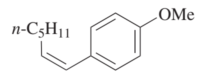
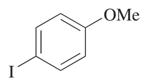
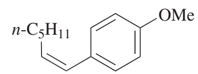
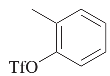
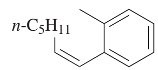
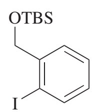
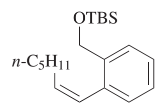
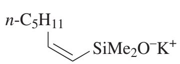
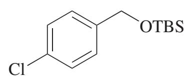
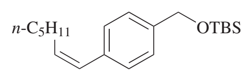
 150%		SPhos (5%), $[\text{allylPdCl}]_2$ (2.5%), THF, 60°, 0.5 h		(98) (*E*)/(*Z*) = 99.5:0.5	80
 150%		SPhos (5%), $[\text{allylPdCl}]_2$ (2.5%), THF, 60°, 1.5 h		(92) (*Z*)/(*E*) = 98.6:1.4	80
 110%		Pd(dba)_2 (5%), TBAF (300%), THF, rt, 10 min		(90) (*E*)/(*Z*) = 99.1:0.9	38
 110%		Pd(dba)_2 (5%), TBAF (200%), THF, rt, 10 min		(90) (*Z*)/(*E*) = 97.3:2.7	31
		Pd(dba)_2 (5%), KOTMS (200%), DME, rt, 7.5		(86) (*Z*)/(*E*) = 98.2:1.8	32
 110%		Pd(dba)_2 (5%), TBAF (200%), THF, rt, 10 min		(81) (*Z*)/(*E*) = 99.4:0.6	31
		Pd(dba)_2 (5%), KOTMS (200%), DME, rt, 0.25 h		(85) (*Z*)/(*E*) = 96.2:3.8	32
 150%		SPhos (5%), $[\text{allylPdCl}]_2$ (2.5%), THF, 66°, 3 h		(96) (*Z*)/(*E*) = 99.5:0.5	80

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 (90) (*Z*)/(*E*) = 97.5:2.5	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (94) (*Z*)/(*E*) = 97.4:2.6	31
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 9.5 h	 (91) (*Z*)/(*E*) = 98.9/1.1	32
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min	 (80)	320
110%		JohnPhos (10%), $PdBr_2$ (5%), TBAF•$6H_2O$ (200%), dioxane, rt, 25 h	 (86) (*Z*)/(*E*) = 99.6:0.4	202
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 14.5h	 (76) (*Z*)/(*E*) = 98.0:2.0	32
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1.5 h	 (98) (*Z*)/(*E*) = 99.6:0.4	80

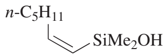
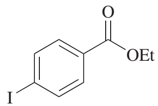
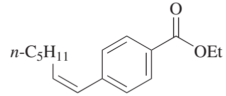
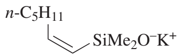
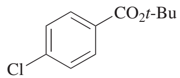
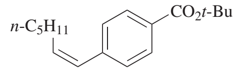
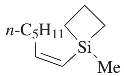
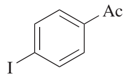
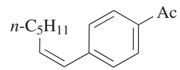
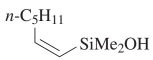
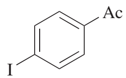
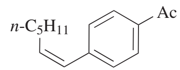
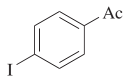
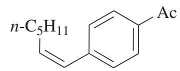
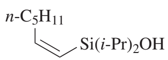
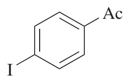
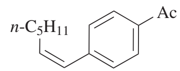
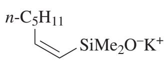
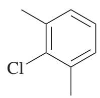
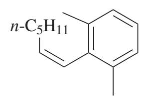
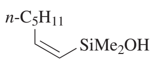
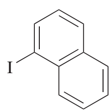
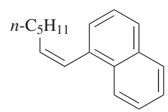
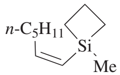
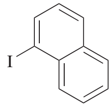
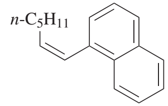
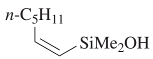
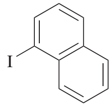
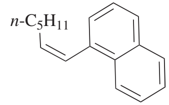
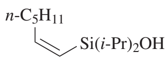
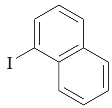
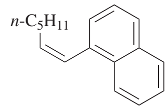
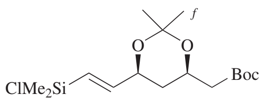
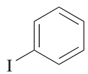
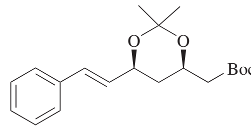
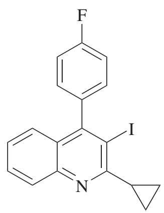
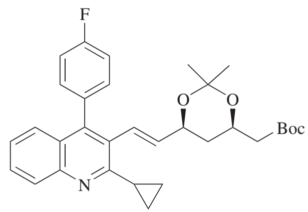
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 0.25 h		(83) $(Z)/(E)$ = 99.3:0.7	32
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 0.33 h		(97) $(Z)/(E)$ = 98.8:1.2	80
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min		(88) $(Z)/(E)$ = 98:2	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(92) $(Z)/(E)$ = 95.2:4.8	31
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 13 h		(83) $(Z)/(E)$ = 97.1:2.9	32
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(86) $(Z)/(E)$ = 99.0:1.0	38
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 2 h		(87) $(Z)/(E)$ = 99.8:0.2	80
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min		(85) $(Z)/(E)$ = 96.7:3.3	31

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 30 min		(91) (*Z*)/(*E*) = 98.5:1.5	38
		$Pd(dba)_2$ (5%), KOTMS (200%), DME, rt, 9 h		(88) (*Z*)/(*E*) = 97.2:2.8	32
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 30 min		(79) (*Z*)/(*E*) = 97.7:2.3	31
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 0.5 h		(81) (*E*)/(*Z*) = 96:4	177
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 0.5 h		(83) (*E*)/(*Z*) = 96:4	177

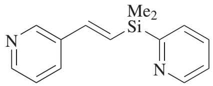
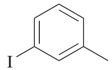
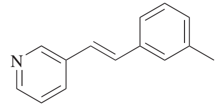
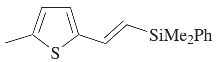
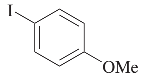
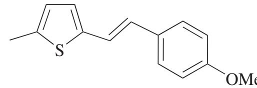
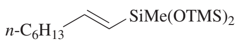
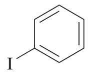
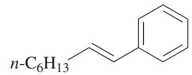
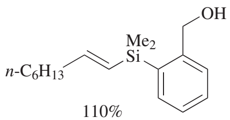
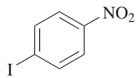
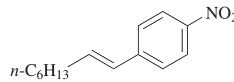
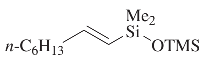
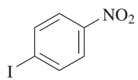
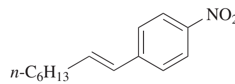
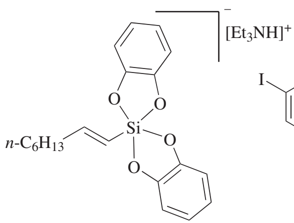
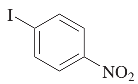
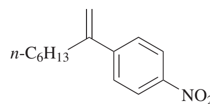
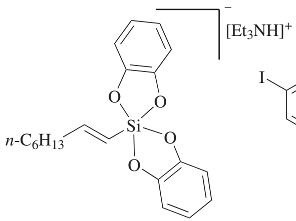
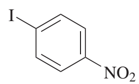
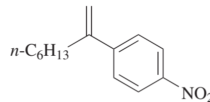
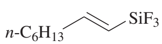
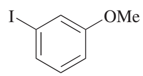
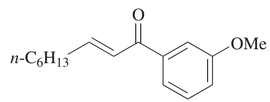
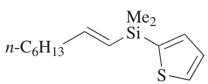
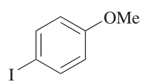
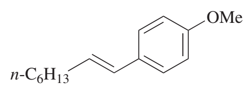
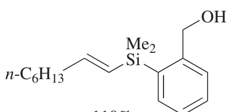
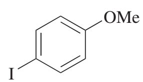
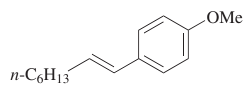
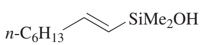
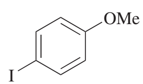
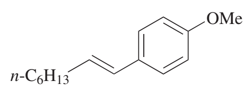
	 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°	 (97)	170
			$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 65°, 12 h	 (57)	162
C_8			$Pd_2(dba)_3$ (1%), TBAF (200%), THF, 20°, 1 h	 (93)	321
	 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 26 h	 (99)	150, 151
	 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3 \bullet CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min	 (81) (*E*)/(*Z*) > 99:1	230
			$[allylPdCl]_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 110 h	 (51)	87

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$PdCl_2(PhCN)_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 110 h		(33)	22
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), CO (1 atm), THF, 50°, 17 h		(71)	179
 120% (*E*)/(*Z*) = 99:1		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 0.5 h		(97) (*E*)/(*Z*) = 99:1	49
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 35°, 40 h		(89)	150, 151
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 4 h		(95)	37

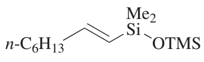
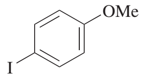
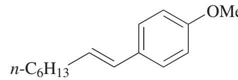
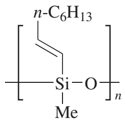
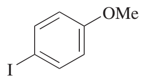
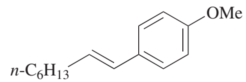
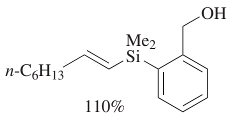
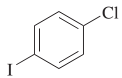
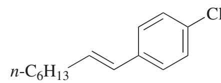
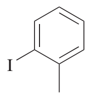
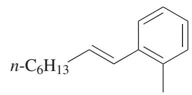
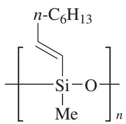
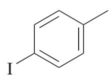
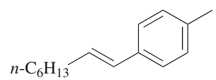
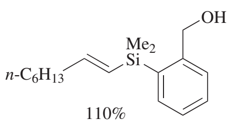
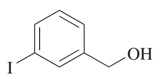
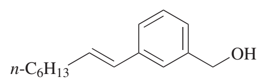
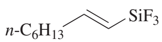
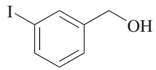
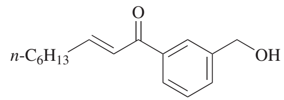
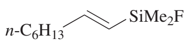
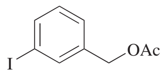
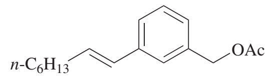
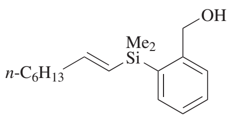
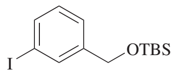
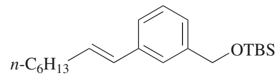
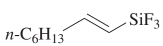
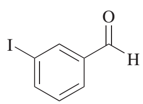
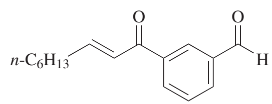
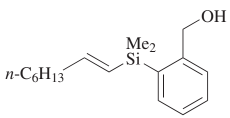
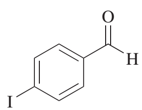
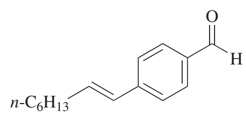
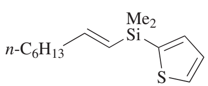
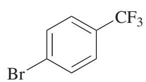
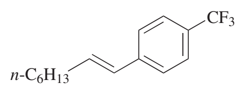
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(95) (*E*)/(*Z*) > 99:1	230
 120%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 1 h		(98)	268
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 19 h		(93)	150, 151
110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 47 h		(94)	150, 151
 500%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 1 h		(51)	268
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 47 h		(88)	150, 151

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), CO (1 atm), THF, 50°, 17 h	 (43)	179
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 24 h	 (85)	25
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 23 h	 (98)	150, 151
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), CO (1 atm), THF, 50°, 17 h	 (66)	179
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 20 h	 (94)	150, 151
 120% (*E*)/(*Z*) = 99:1		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 5 h	 (96) (*E*)/(*Z*) = 97:3	49

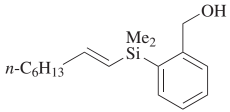
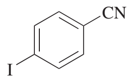
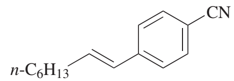
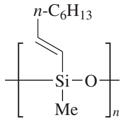
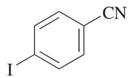
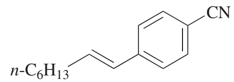
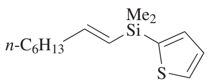
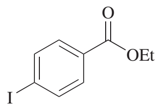
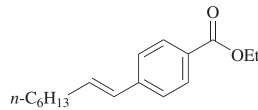
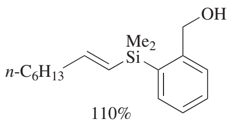
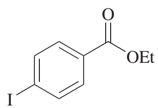
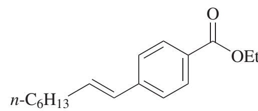
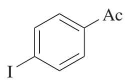
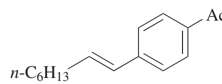
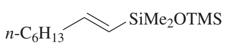
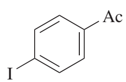
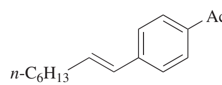
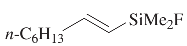
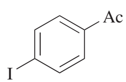
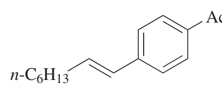
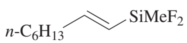
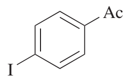
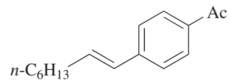
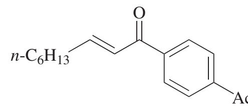
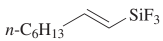
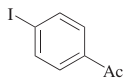
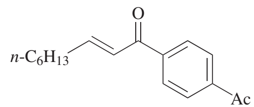
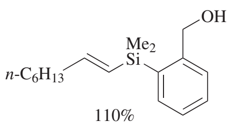
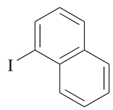
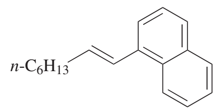
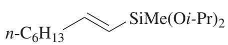
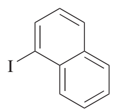
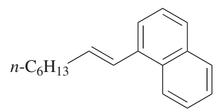
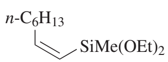
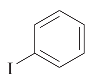
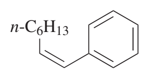
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 20 h		(93)	150, 151
 500%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 2 h		(90)	268
 120% (*E*)/(*Z*) = 99:1		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 0.5 h		(94) (*E*)/(*Z*) = 99:1	49
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 18 h		(96)	150, 151
110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 17 h		(94)	150, 151
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(86) (*E*)/(*Z*) > 99:1	230
		[allylPdCl]$_2$ (2.5%), TASF (150%), THF, 24 h		(78)	25

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 150%		$[allylPdCl]_2$ (2.5%), TBAF (300%), CO (1 atm), THF, 50°, 12 h	 (52) +  (42)	179
 150%		$[allylPdCl]_2$ (2.5%), TBAF (300%), CO (1 atm), THF, 50°, 22 h	 (85)	179
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 23 h	 (91)	150, 151
	 110%	$[allylPdCl]_2$ (2.5%), (EtO)$_3$P (5%), TBAF (150%), THF, 50°, 5 h	 (91)	26
 120% (*Z*)/(*E*) = 97:3		$[allylPdCl]_2$ (2.5%), Ph_3P (5%), TBAF (200%), THF, rt, 19 h	 (99) (*Z*)/(*E*) > 95:5	230

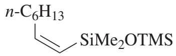
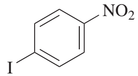
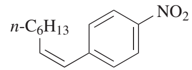
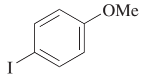
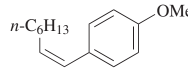
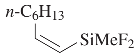
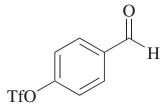
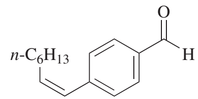
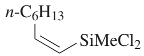
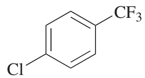
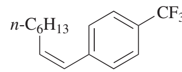
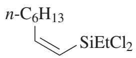
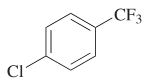
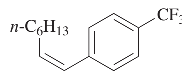
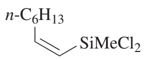
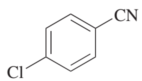
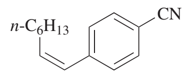
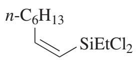
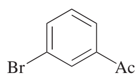
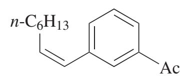
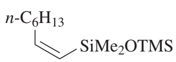
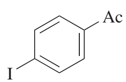
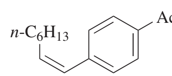
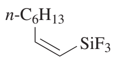
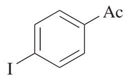
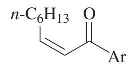
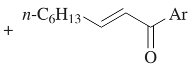
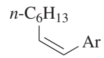
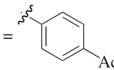
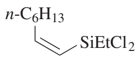
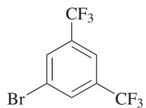
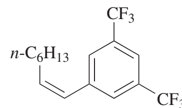
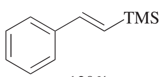
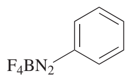
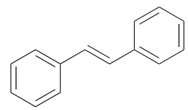
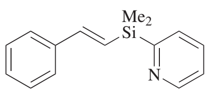
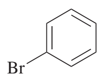
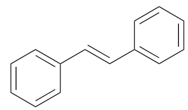
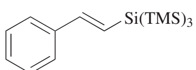
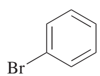
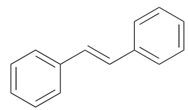
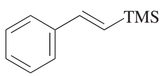
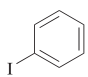
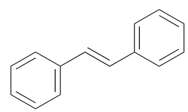
 120% (*Z*)/(*E*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(76) (*Z*)/(*E*) > 99:1	230
120% (*Z*)/(*E*) = 94:5		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(82) (*Z*)/(*E*) = 94:5	230
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 5 h		(73)	181
 120%		$(Et_3P)_2PdCl_2$ (0.5%), TBAF (300%), THF, 90°, 20 h		(58)	187
 120%		(dpce)PdCl (2.5%), NaOH (600%), C_6H_6, 80°, 12 h		(55)	185
 120%		$(Et_3P)_2PdCl_2$ (0.5%), TBAF (300%), THF, 90°, 20 h		(91)	187
 120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 12 h		(70)	185
 120% (*Z*)/(*E*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(93) (*Z*)/(*E*) > 99:1	230

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), CO (1 atm), THF, 50°, 12 h	 (44) +  (26) +  (21) Ar = 	179
 120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 12 h	 (66)	185
 120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (80)	124
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (59)	169
 120%		1. H_2O_2, NaOH, H_2O/THF, 1 h 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), 40°	 (55)	322
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 21 h	 (34)	89

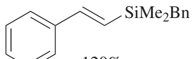
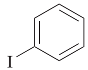
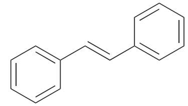
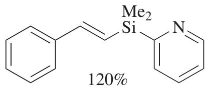
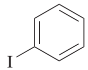
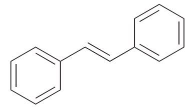
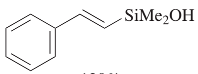
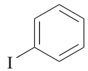
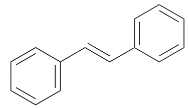
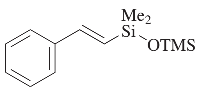
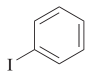
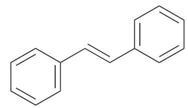
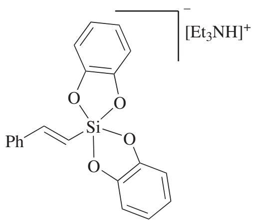
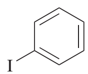
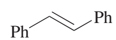
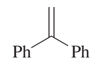
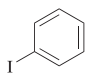
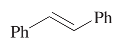
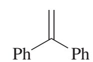
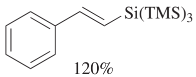
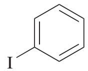
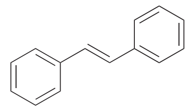
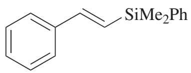
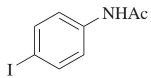
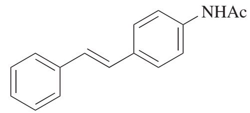
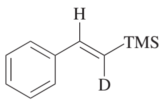
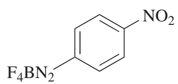
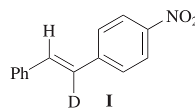
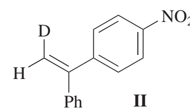
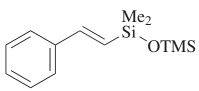
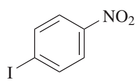
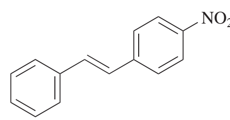
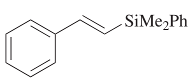
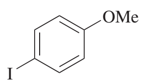
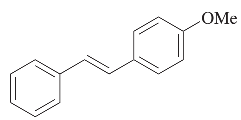
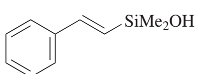
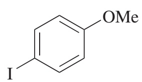
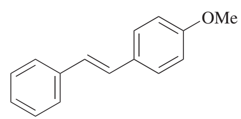
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (91)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (91)	169
 120%		$(Ph_3P)_4P$ (5%), Ag_2O (100%), THF, 60°, 7 h	 (91)	203
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min	 (99) (*E*)/(*Z*) > 99:1	230
		$[allylPdCl]_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 110 h	 (48) +  (25)	22, 87
		$PdCl_2(PhCN)_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 60 h	 (32) +  (13)	87

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 120%		1. H_2O_2, NaOH, H_2O/THF, 1 h 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), 40°	 (75)	322
		$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 65°, 120 h	 (34)	162
 86% D		$Pd(dba)_2$ (5%)	 +  **I** + **II** (86), **I**:**II** = 89:11	93
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3 \bullet CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min	 (84) (*E*)/(*Z*) > 99:1	230
		$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 65°, 48 h	 (67)	162
 120%		$(Ph_3P)_4P$ (5%), Ag_2O (100%), THF, 60°, 7 h	 (89)	203

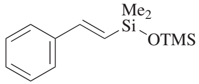
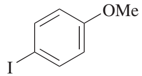
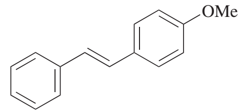
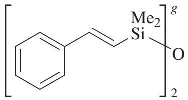
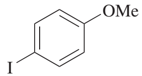
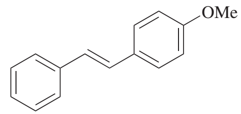
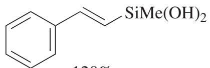
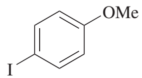
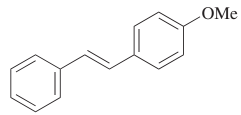
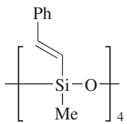
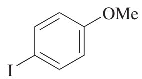
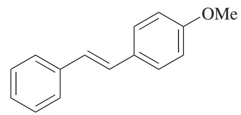
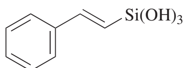
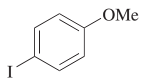
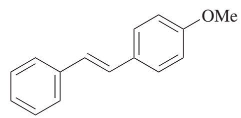
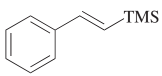
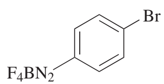
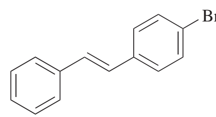
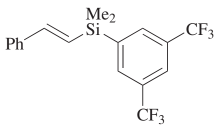
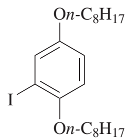
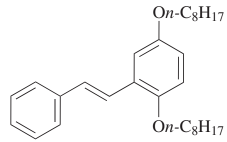
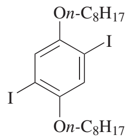
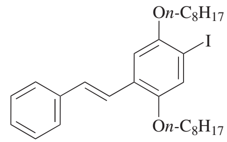
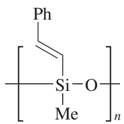
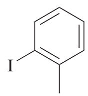
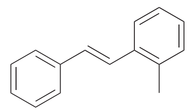
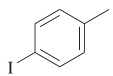
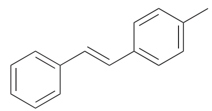
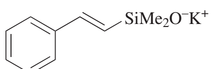
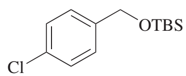
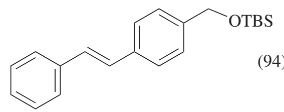
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3 \bullet CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(90) (*E*)/(*Z*) > 99:1	230
 150%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(74)	261
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 12 h		(95)	37
 500%		$Pd_2(dba)_3 \bullet CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 1 h		(99)	268
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 4 h		(76)	37
 120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h		(61)	124

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$[allylPdCl]_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt	 (71)	166
		$[allylPdCl]_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt	 (30)	166
 500%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 1 h	 (97)	268
500%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF (120%), THF, 60°, 1 h	 (99)	268
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), dioxane, 90°, 1.25 h	 (94) (*E*)/(*Z*) = 99.6:0.4	80

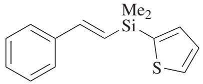
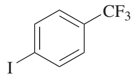
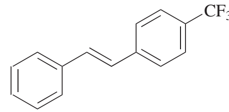
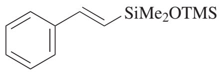
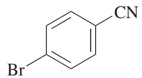
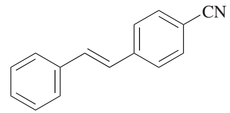
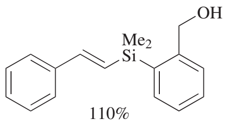
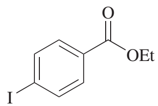
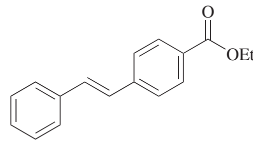
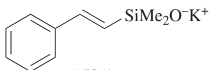
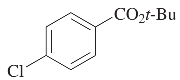
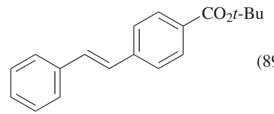
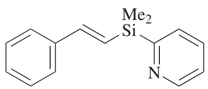
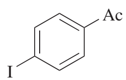
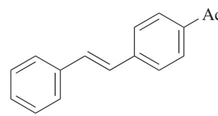
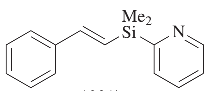
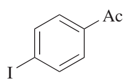
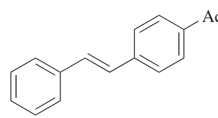
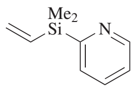
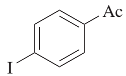
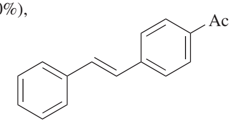
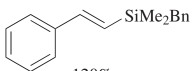
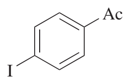
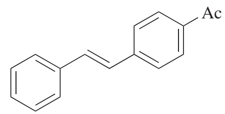
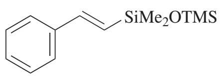
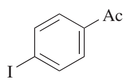
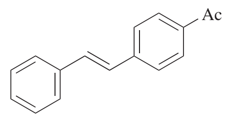
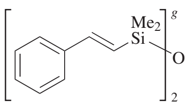
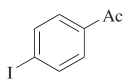
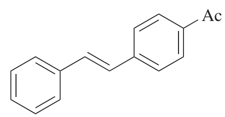
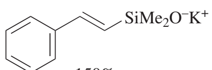
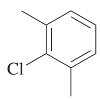
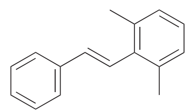
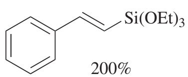
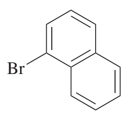
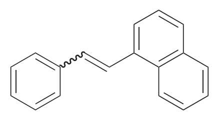
 120% $(E)/(Z) = 99:1$		$Pd(OAc)_2$ (5%), TBAF (120%), THF, rt, 1 h	 (98) $(E)/(Z) = 99:1$	49
 120% $(E)/(Z) > 99:1$		$[allylPdCl]_2$ (2.5%), Ph_3P (5%), TBAF (200%), THF, rt, 22 h	 (57) $(E)/(Z) > 99:1$	230
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 35°, 19 h	 (88)	150, 151
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), dioxane, 90°, 0.5 h	 (89) $(E)/(Z) = 99.9:0.1$	80
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°	 (84)	170
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (84)	169

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 150%		1. PhI (130%), $Pd(OAc)_2$ (10%), $(2\text{-furyl})_3P$ (10%), Et_3N (160%), THF, 60° 2. Electrophile, TBAF (230%)	 (69)	170
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°	 (84)	169
 120% (*E*)/(*Z*) > 99:1		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min	 (85) (*E*)/(*Z*) > 99:1	230
 150%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min	 (89)	261
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), dioxane, 90°, 1.25 h	 (91) (*E*)/(*Z*) = 99.7:0.3	80
 200%		Pd cat. **5**, (1%), NaOH (250%), TBAB (100%), H_2O, MW, 120°, 20 min	 (83) (*E*)/(*Z*) = 1.9:1	257

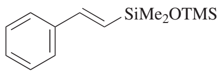
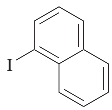
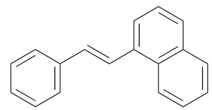
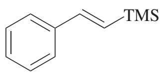
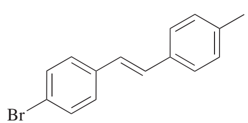
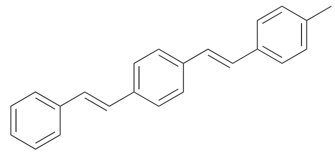
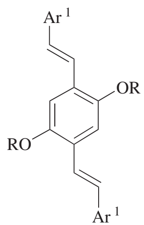
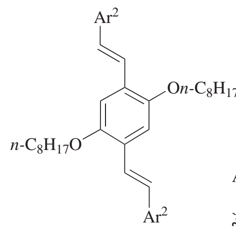
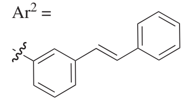
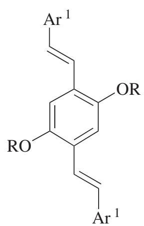
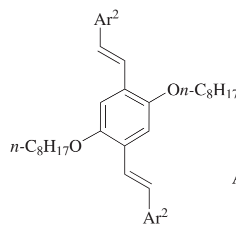
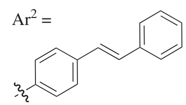
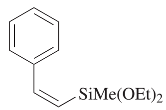
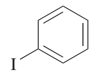
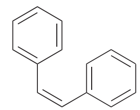
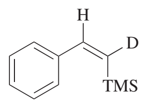
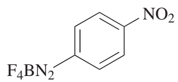
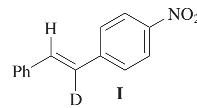
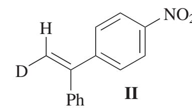
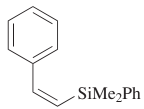
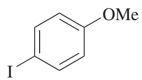
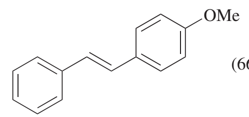
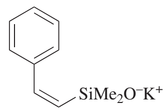
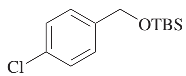
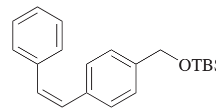
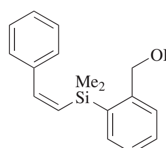
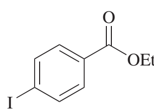
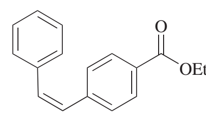
 120% $(E)/(Z) > 99:1$		$Pd_2(dba)_3 \cdot CHCl_3$ (5%), TBAF (200%), THF, rt, 10 min		(94) $(E)/(Z) > 99:1$	230
		1. BCl_3, CH_2Cl_2, 0° 2. Aryl bromide, $(Ph_3P)_4Pd$ (cat.), aq. NaOH, benzene, reflux		(78)	90
216%	 R = n-C_8H_{18} Ar[1] = 3-BrC_6H_4	1. BCl_3, CH_2Cl_2, 0° 2. H_2O, Na_2CO_3 3. Electrophile, $(Ph_3P)_4Pd$ (20%), Na_2CO_3, toluene, MeOH, reflux	 Ar^2 = 	(94)	91
216%	 R = n-C_8H_{18} Ar[1] = 4-BrC_6H_4	1. BCl_3, CH_2Cl_2, 0° 2. H_2O, Na_2CO_3 3. Electrophile, $(Ph_3P)_4Pd$ (20%), Na_2CO_3, toluene, MeOH, reflux	 Ar^2 = 		91

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 120% (*Z*)/(*E*) = 98:2		$[allylPdCl]_2$ (2.5%), Ph_3P (5%), TBAF (200%), THF, 60°, 6 h	 (86) (*Z*)/(*E*) = 91:9	230
 97% D		$Pd(dba)_2$ (5%)	 I +  II **I** + **II** (91), **I**:**II** = 83:17	93
		$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 65°, 48 h	 (66)	162
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), dioxane, 90°, 1.25 h	 (97) (*Z*)/(*E*) = 99.5:0.5	80
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 35°, 11 h	 (92)	150

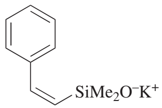
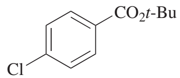
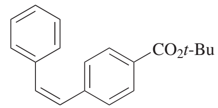
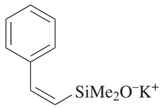
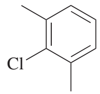
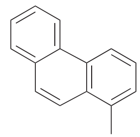
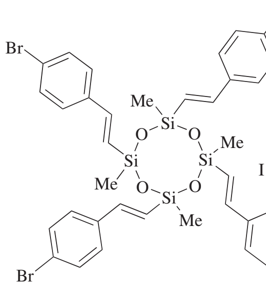
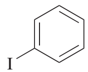
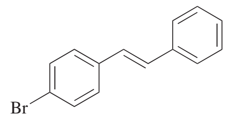
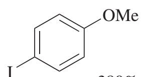
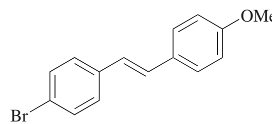
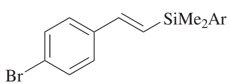
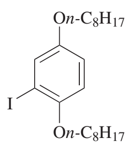
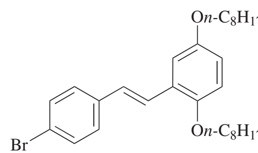
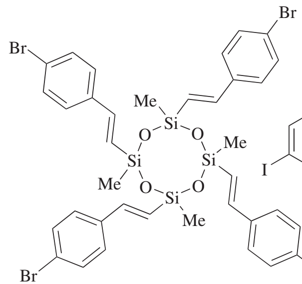
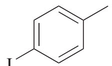
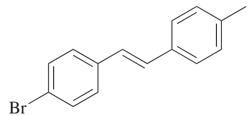
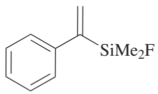
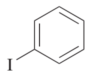
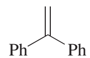
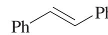
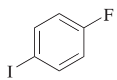
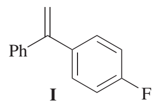
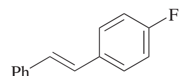
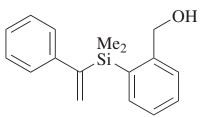
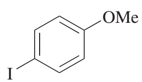
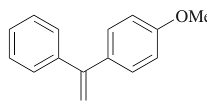
 150%		SPhos (5%), [allylPdCl]$_2$ (2.5%), dioxane, 90°, 0.5 h		(94) $(Z)/(E)$ = 99.5:0.5	80
 150%		SPhos (5%), [allylPdCl]$_2$ (2.5%), dioxane, 90°, 1.25 h		(90) $(Z)/(E)$ = 99.7:0.3	80
	 380%	Pd(dba)$_2$ (5%), TBAF (800%), THF, 65°		(85)	266
	 380%	Pd(dba)$_2$ (5%), TBAF (800%), THF, 65°		(88)	266
 Ar = 3,5-$(CF_3)_2C_6H_3$		[allylPdCl]$_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt		(75)	166

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 380%	$Pd(dba)_2$ (5%), TBAF (800%), THF, 65°	 (92)	266
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 4 h	 **I** +  **II** **I** + **II** (69), **I**:**II** = 75:25	89
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 4 h	 **I** +  **II** **I** + **II** (80), **I**:**II** = 79:21	89
 130%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 50°, 12 h	 (80)	150, 151

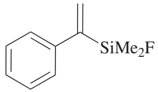
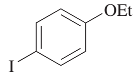
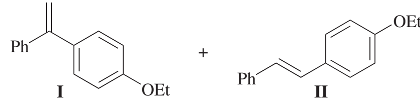
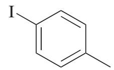
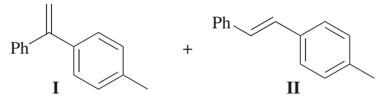
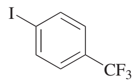
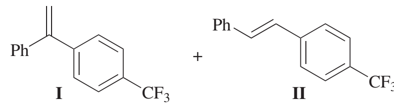
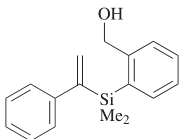
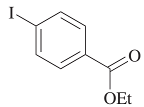
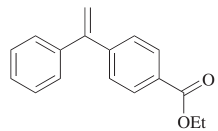
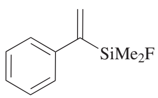
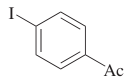
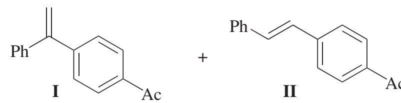
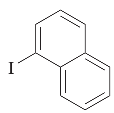
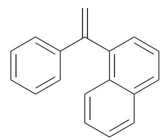
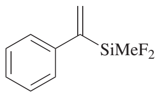
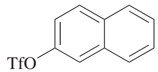
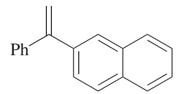
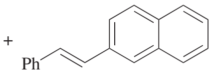
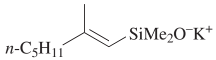
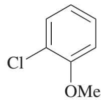
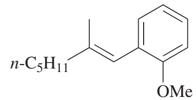
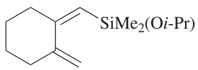
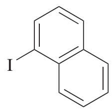
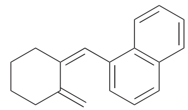
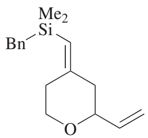
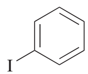
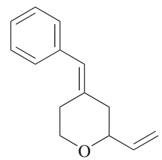
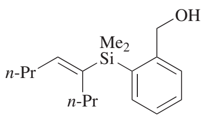
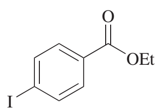
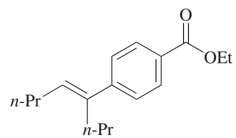
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 20 h	 **I** + **II** (63), **I**:**II** = 60:40	89
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 14 h	 **I** + **II** (84), **I**:**II** = 59:21	89
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 24 h	 **I** + **II** (72), **I**:**II** = 97:3	89
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 25 h	 (95)	150, 151
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 20 h	 **I** + **II** (73), **I**:**II** = 88:12	89
		$[allylPdCl]_2$ (2.5%), TBAF (110%), THF, 60°, 21 h	 (74)	89

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 5 h	 (50) +  (26)	181
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 66°, 1 h	 (98) (*E*)/(*Z*) > 99:1	80
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 7 h	 (79) (*Z*)/(*E*) = 95:5	26
	 150%	$Pd_2(dba)_3$ $CHCl_3$ (2%), TBAF (200%), THF, 23°, 2.5 h	 (85)	323
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (220%), DMSO, 50°, 29 h	 (92)	150, 151

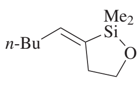
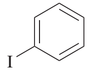
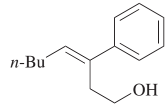
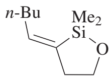
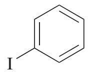
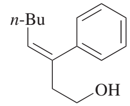
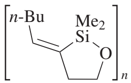
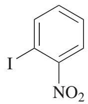
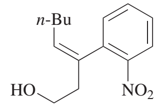
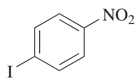
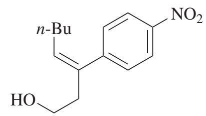
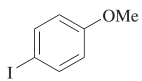
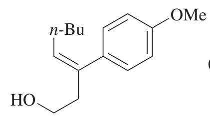
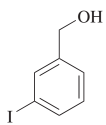
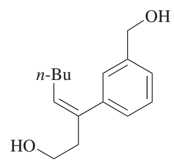
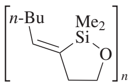
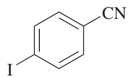
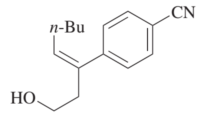
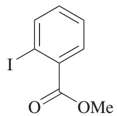
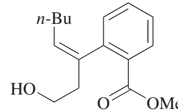
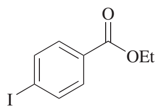
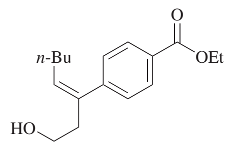
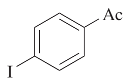
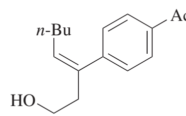
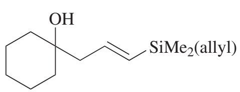
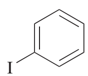
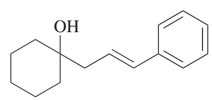
 [h] 130%		TBAF (220%), Pd(dba)$_2$ (5%), THF, rt, 90 min		(85) $(E)/(Z)$ = 98.3:1.7	224
		1. TBAF (150%) 2. Pd(dba)$_2$ (5%), dioxane, 45°, 8.1 h		(65) $(E)/(Z)$ = 95.3:4.7	198
		1. TBAF (150%) 2. Pd(dba)$_2$ (5%), dioxane, rt, 7 h; then 35°, 47 h		(66) $(Z)/(E)$ = 96.2:3.8	198
		1. TBAF (150%) 2. Pd(dba)$_2$ (5%), dioxane, 45°, 7.6 h		(68) $(Z)/(E)$ = 96.4:3.6	198
		1. TBAF (150%) 2. Pd(dba)$_2$ (5%), dioxane, rt, 41 h		(60) $(Z)/(E)$ = 99.3:0.7	198
		1. TBAF (150%) 2. Pd(dba)$_2$ (5%), dioxane, rt, 13.5 h, then 45°, 33 h		(59) $(Z)/(E)$ = 98.4:1.6	198

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		1. TBAF (150%) 2. $Pd(dba)_2$ (5%), dioxane, 45°, 25.5 h	 (64)	198
		1. TBAF (150%) 2. $Pd(dba)_2$ (5%), dioxane, 35°, 43 h	 (64) (*Z*)/(*E*) = 95:5	198
		1. TBAF (150%) 2. $Pd(dba)_2$ (5%), dioxane, 40°, 15.5 h	 (72) (*Z*)/(*E*) = 96.5:3.5	198
		1. TBAF (150%) 2. $Pd(dba)_2$ (5%), dioxane, rt, 46 h	 (66) (*Z*)/(*E*) = 97.4:2.6	198
C_9				
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile	 (83)	157

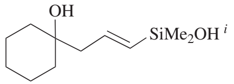
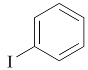
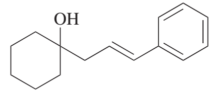
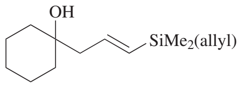
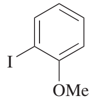
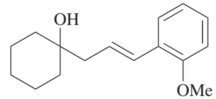
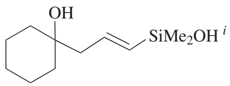
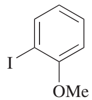
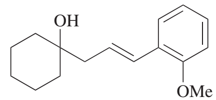
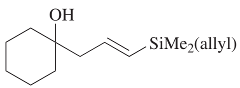
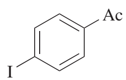
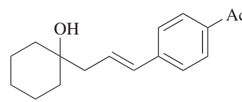
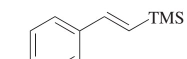
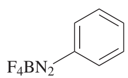
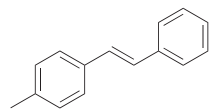
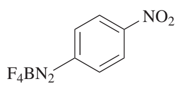
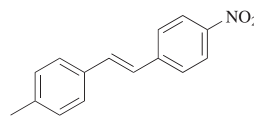
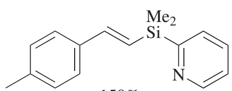
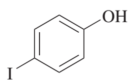
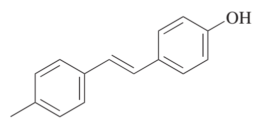
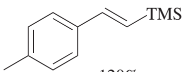
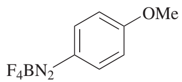
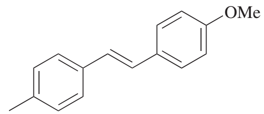
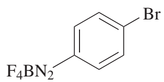
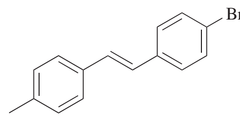
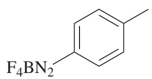
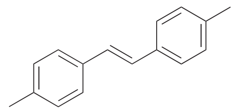
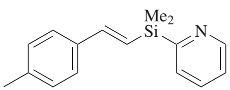
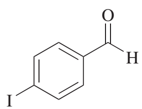
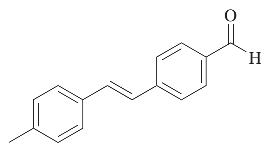
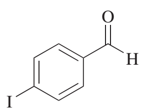
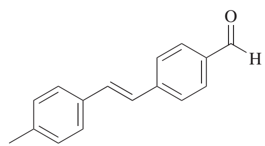
		$Pd_2(dba)_3$ (cat.), TBAF, electrophile, THF, rt	 (62)	222
		1. TBAF (200%), $[allylPdCl]_2$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile	 (60)	157
		$Pd_2(dba)_3$ (cat.), TBAF, electrophile, THF, rt	 (41)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile	 (83)	157
 120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (72)	124
120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (58)	124
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°	 (85)	170

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
 120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (65)	124
120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (60)	124
120%		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h	 (62)	124
 150%		1. $Pd(OAc)_2$ (10%), $(2\text{-furyl})_3P$ (10%), Et_3N (160%), THF, 60° 2. Electrophile, TBAF (230%)	 (92)	170
150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°	 (91)	170

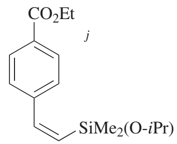
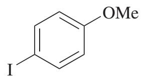
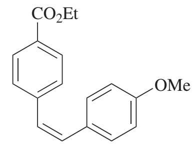
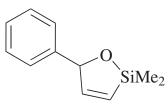
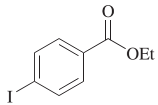
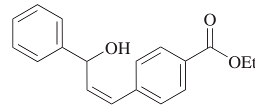
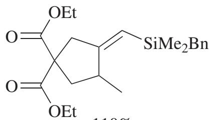
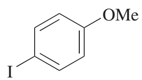
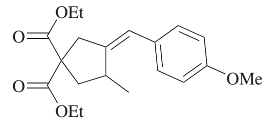
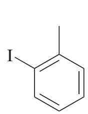
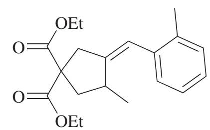
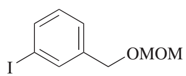
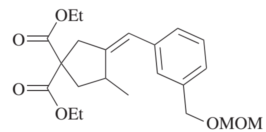
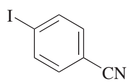
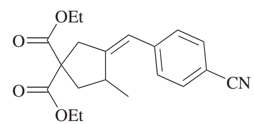
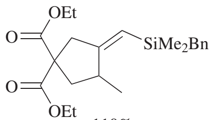
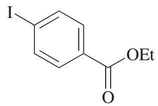
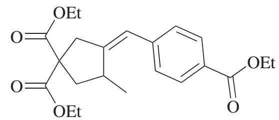
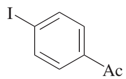
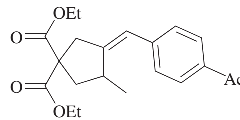
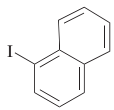
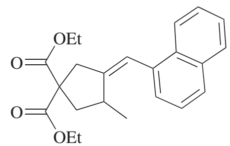
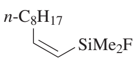
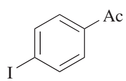
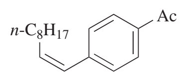
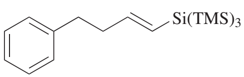
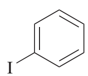
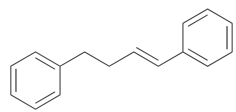
 111%		PdCl(PPh$_3$)(Bn) (5%), CuI (10%), TBAF (278%), DMF, 50°, 8 h		(65)	128
		Pd(dba)$_2$ (3%), TBAF (200%), THF, rt, 30 min		(85)	225, 226
 110%		Pd$_2$(dba)$_3$•CHCl$_3$ (2.5%), TBAF•3H$_2$O (200%), THF, rt		(82)	45
110%		Pd$_2$(dba)$_3$•CHCl$_3$ (2.5%), TBAF•3H$_2$O (200%), THF, rt		(81)	45
110%		Pd$_2$(dba)$_3$•CHCl$_3$ (2.5%), TBAF•3H$_2$O (200%), THF, rt		(85)	45
110%		Pd$_2$(dba)$_3$•CHCl$_3$ (2.5%), TBAF•3H$_2$O (200%), THF, rt		(76)	45

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt	 (90)	45
110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt	 (86)	45
110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, rt	 (85)	45
C_{10}				
		$(Ph_3P)_4Pd$ (5%), TASF (150%), DMF, 12 h	 (79)	25
		1. H_2O_2, NaOH, H_2O/THF, 1 h 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), 40°	 (56)	322

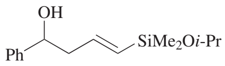
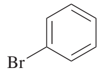
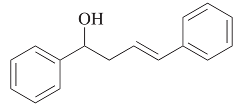
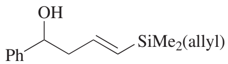
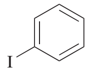
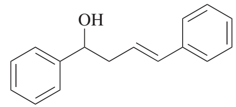
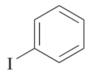
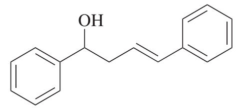
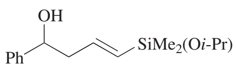
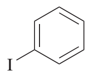
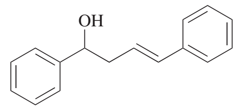
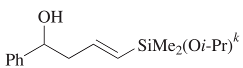
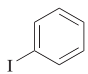
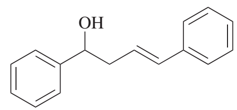
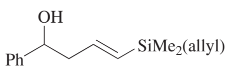
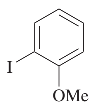
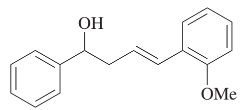
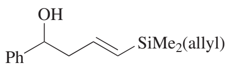
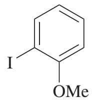
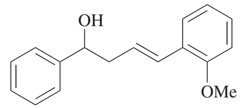
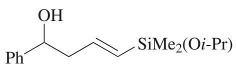
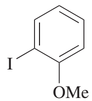
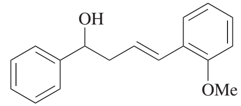
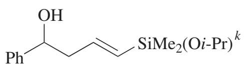
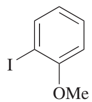
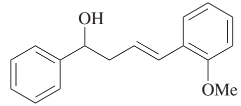
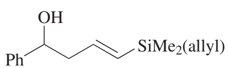
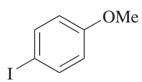
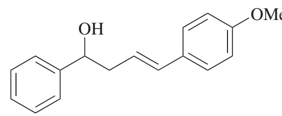
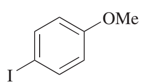
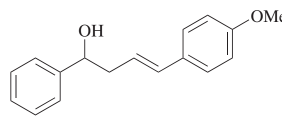
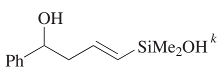
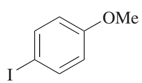
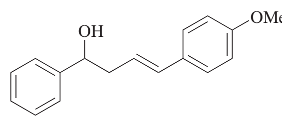
		[allylPdCl]$_2$ (cat.), TBAF (200%), THF, 50°, 24 h		(82)	222
		1. TBAF (200%), Pd$_2$(dba)$_3$ (cat.), EtOH (600%), THF, rt, 30 min 2. Electrophile		(91)	157
		1. TBAF (200%), Pd$_2$(dba)$_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(91)	157
		Pd$_2$(dba)$_3$ (cat.), TBAF (200%), THF, rt, 4 h		(97)	222
		Pd$_2$(dba)$_3$ (5%), TBAF (240%), electrophile (70%)		(90)	222
		1. TBAF (200%), [allylPdCl]$_2$ (cat.), EtOH (600%), THF, rt, 30 min 2. Electrophile		(63)	157

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}					
		1. TBAF (200%), $[allylPdCl]_2$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(63)	157
		$[allylPdCl]_2$ (cat.), TBAF (200%), THF, rt, 1.5 h		(93)	222
 [k]		$[allylPdCl]_2$ (5%), TBAF (240%), electrophile (70%)		(65)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (cat.), EtOH (600%), THF, rt, 30 min 2. Electrophile		(78)	157
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(78)	157
 [k]		$[allylPdCl]_2$ (5%), TBAF (240%), electrophile (70%)		(86)	222

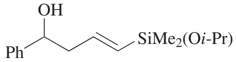
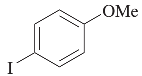
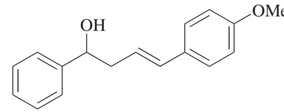
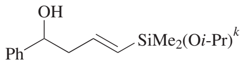
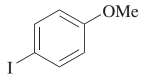
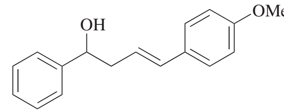
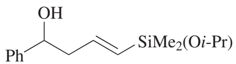
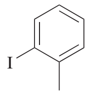
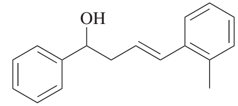
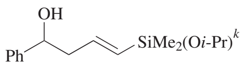
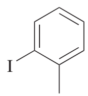
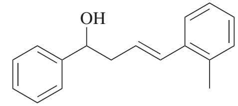
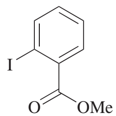
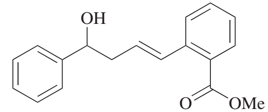
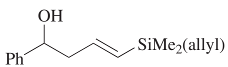
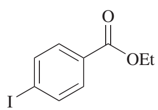
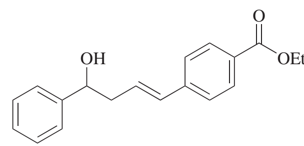
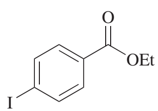
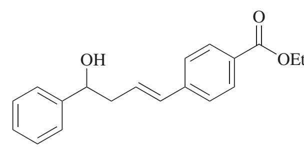
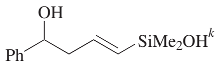
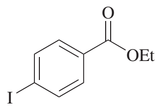
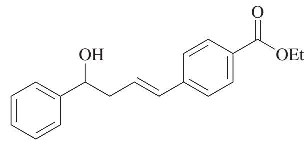
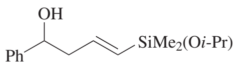
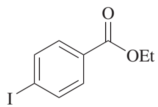
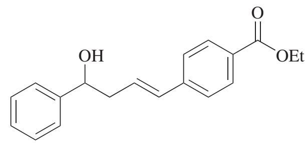
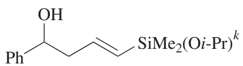
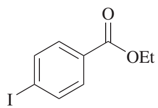
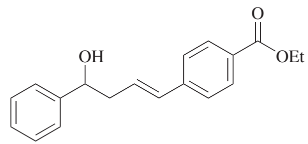
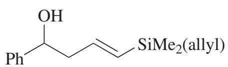
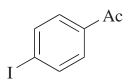
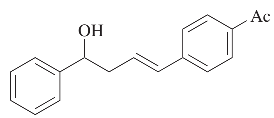
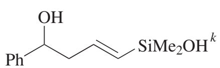
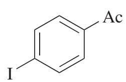
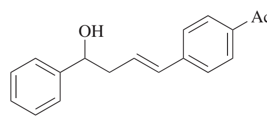
		$Pd_2(dba)_3$ (cat.), TBAF (200%), THF, rt, 4 h		(90)	222
		$[allylPdCl]_2$ (5%), TBAF (240%), electrophile (70%)		(86)	222
		$[allylPdCl]_2$ (cat.), TBAF (200%), THF, rt, 3 h		(99)	222
		$[allylPdCl]_2$ (5%), TBAF (240%), electrophile (70%)		(63)	222
		$[allylPdCl]_2$ (5%), TBAF (240%), electrophile (70%)		(56)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (cat.), EtOH (600%), THF, rt, 30 min 2. Electrophile		(85)	157
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(85)	157

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}					
		$Pd_2(dba)_3$ (5%), TBAF (240%), electrophile (70%)		(89)	222
		$Pd_2(dba)_3$ (cat.), TBAF (200%), THF, rt, 3 h		(98)	222
		$Pd_2(dba)_3$ (5%), TBAF (240%), electrophile (70%)		(89)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(84)	157
		$Pd_2(dba)_3$ (5%), TBAF (240%), electrophile (70%)		(91)	222

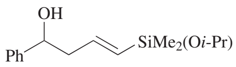
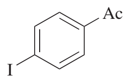
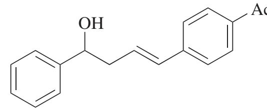
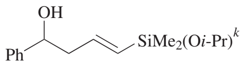
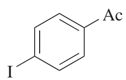
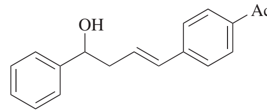
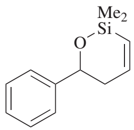
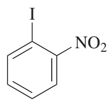
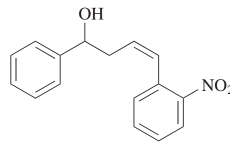
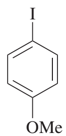
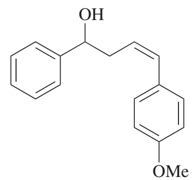
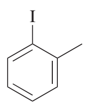
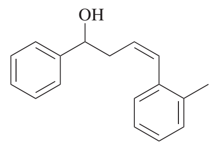
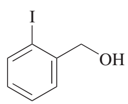
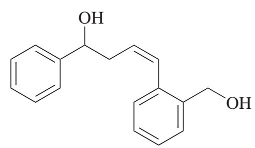
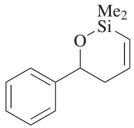
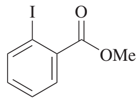
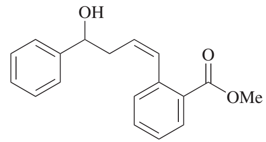
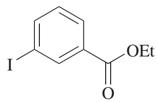
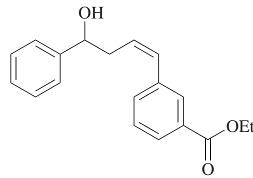
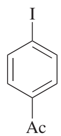
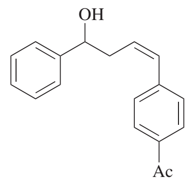
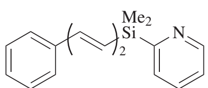
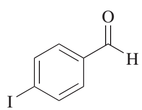
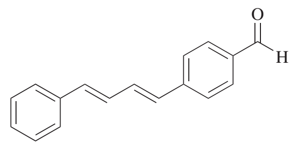
		$Pd_2(dba)_3$ (cat.), TBAF (200%), THF, rt, 4 h		(96)	222
		$Pd_2(dba)_3$ (5%), TBAF (240%), electrophile (70%)		(91)	222
		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 90 min		(86)	225, 226
		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 30 min		(92)	225, 226
		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 30 min		(89)	225, 226
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 180 min		(90)	225, 226

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}					
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 180 min		(84)	225, 226
		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 30 min		(93)	225, 226
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 10 min		(90)	225, 226
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(89)	169

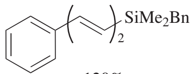
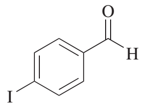
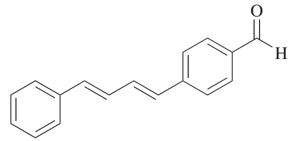
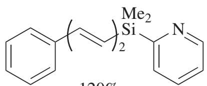
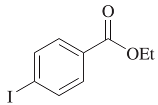
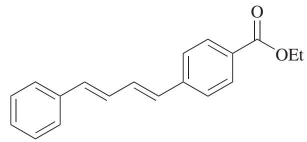
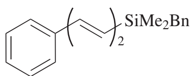
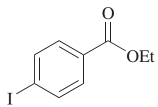
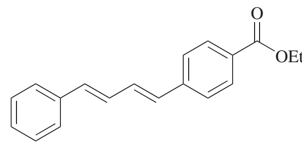
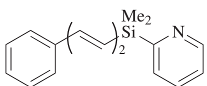
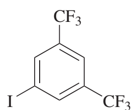
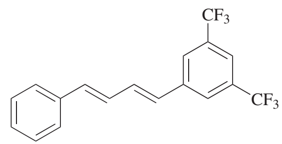
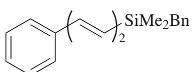
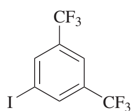
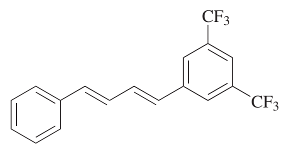
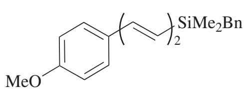
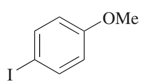
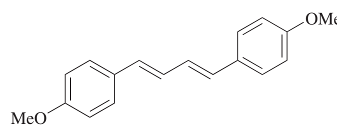
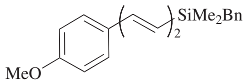
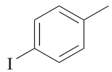
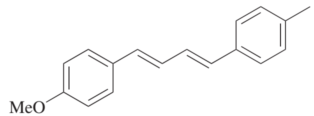
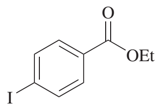
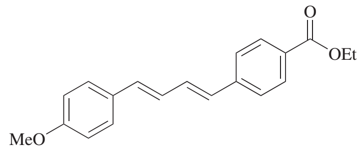
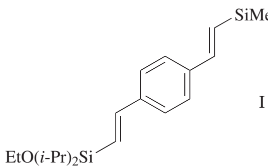
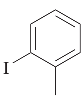
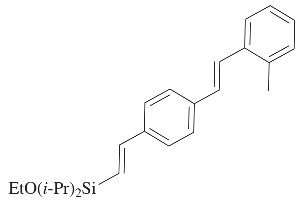
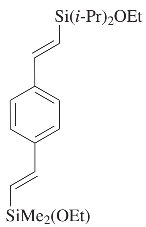
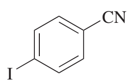
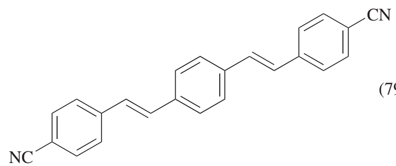
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(89)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(85)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(85)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(73)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(73)	169
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 15 min		(91)	44

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}					
 120%		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 15 min		(86)	44
120%		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 15 min		(88)	44
		$[allylPdCl]_2$ (2.5%), KOTMS (400%), rt		(—)	72
	 210%	$[allylPdCl]_2$ (2.5%), TBAF (400%), rt		(79)	45

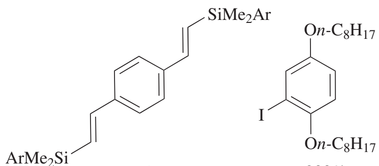
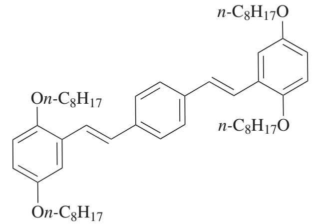
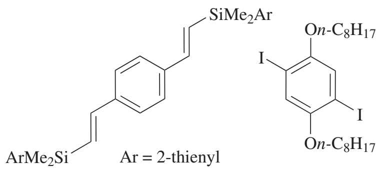
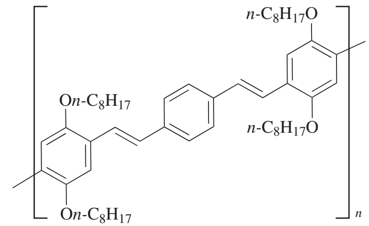
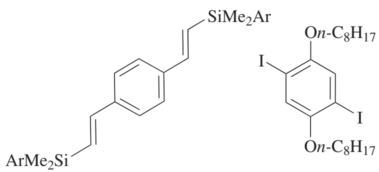
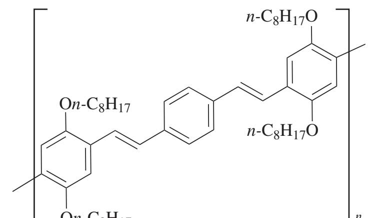
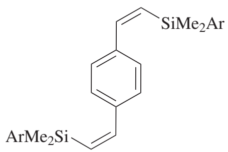
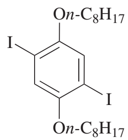
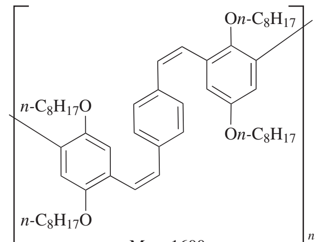
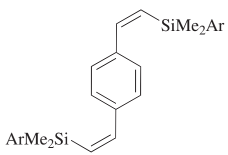
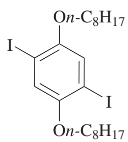
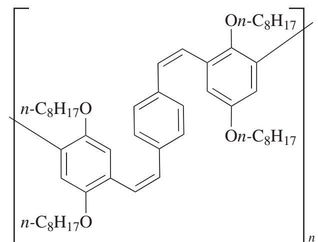
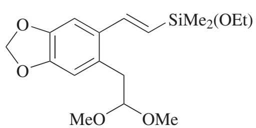
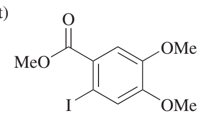
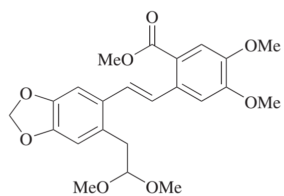
Reactant(s)	Conditions	Product(s) and Yield(s) (%)	Refs.
 Ar = 3,5-$(CF_3)_2C_6H_3$ 200%	$[allylPdCl]_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt, 24 h	 (31)	166
 Ar = 2-thienyl	$[allylPdCl]_2$ (5%), TBAF (200%), THF, rt, 24 h	 M_n = 5700 (>99)	165
 Ar = 3,5-$(CF_3)_2C_6H_3$	$[allylPdCl]_2$ (5%), TBAF (200%), THF, rt, 24 h	 M_n = 6300 (>99)	165

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
 Ar = 2-thienyl		$[allylPdCl]_2$ (5%), TBAF (200%), THF, rt, 24 h	 (97) M_n = 1600 (*Z*)/(*E*) = 55:45	165
 Ar = 3,5-$(CF_3)_2C_6H_3$		$[allylPdCl]_2$ (5%), TBAF (200%), THF, rt, 24 h	 (97) M_n = 1600 (*Z*)/(*E*) = 55:45	165
		$[allylPdCl]_2$ (5%), $(EtO)_3P$ (10%), TBAF (120%), THF, 60°, 2 h	 (—)	285

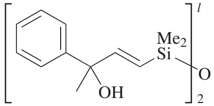
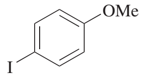
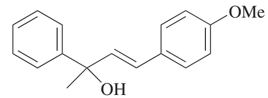
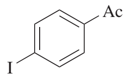
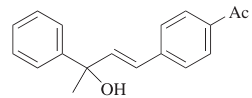
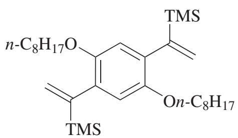
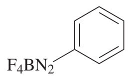
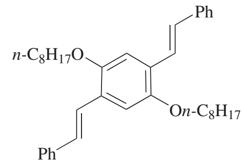
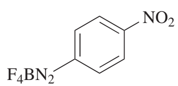
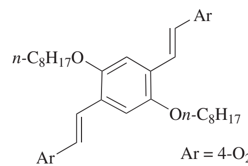
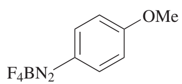
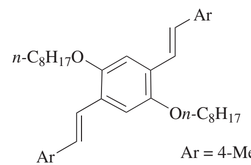
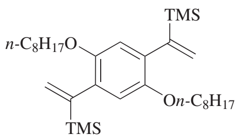
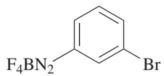
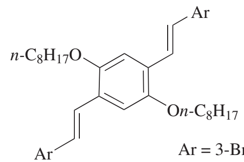
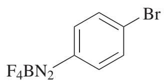
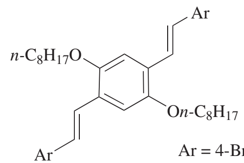
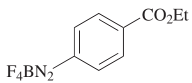
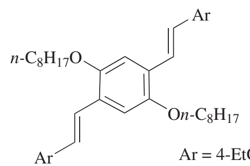
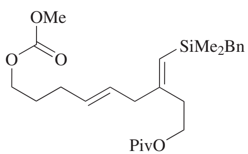
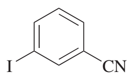
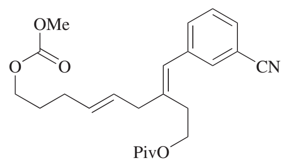
 130%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 24 h		(79)	261
		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 24 h		(72)	261
	 250%	Pd(dba) (25%), MeCN, rt		(56)	91
	 250%	Pd(dba) (25%), MeCN, rt	 Ar = 4-$O_2NC_6H_4$	(45)	91
	 250%	Pd(dba) (25%), MeCN, rt	 Ar = 4-$MeOC_6H_4$	(66)	91

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	 250%	Pd(dba) (25%), MeCN, rt	 Ar = 3-BrC_6H_4 (80)	91
	 250%	Pd(dba) (25%), MeCN, rt	 Ar = 4-BrC_6H_4 (65)	90, 91
	 250%	Pd(dba) (25%), MeCN, rt	 Ar = 4-$EtO_2CC_6H_4$ (83)	91
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h	 (70)	43

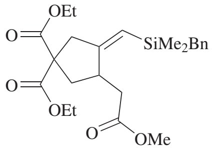
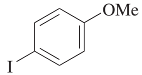
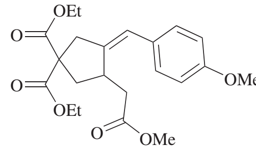
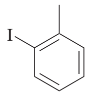
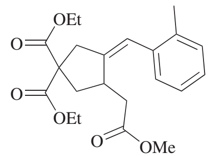
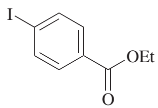
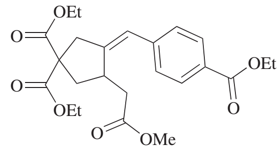
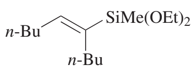
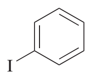
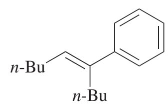
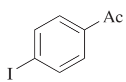
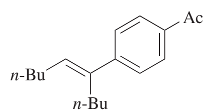
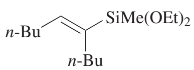
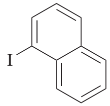
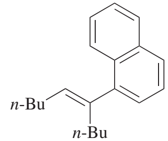
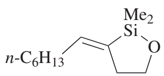
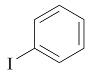
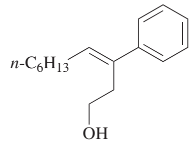
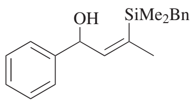
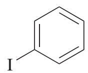
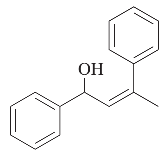
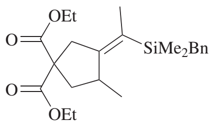
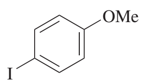
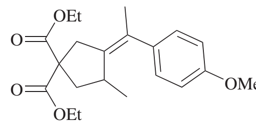
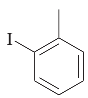
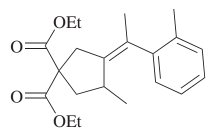
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $TBAF$•$3H_2O$ (200%), THF, rt		(77)	45
		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $TBAF$•$3H_2O$ (200%), THF, rt		(73)	45
		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $TBAF$•$3H_2O$ (200%), THF, rt		(74)	45
	 110%	TBAF (150%), $[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), THF, 50°, 5 h		(90)	26
	 110%	TBAF (150%), $[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), THF, 50°, 5 h		(77)	26

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 5 h	 (96)	26
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°	 (67)	26
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h	 (76)	43
 110%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, 35°	 (74)	45
		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), TBAF•$3H_2O$ (200%), THF, 35°	 (64)	45

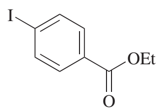
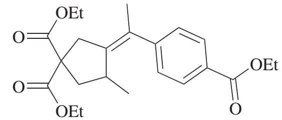
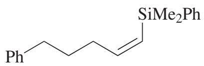
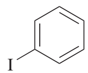
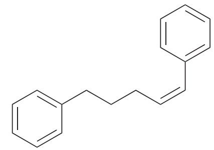
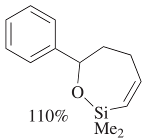
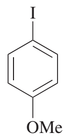
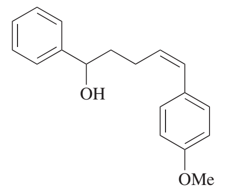
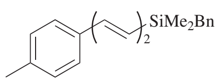
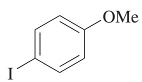
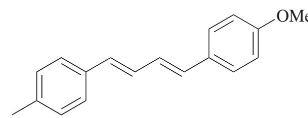
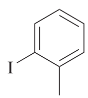
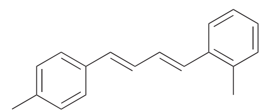
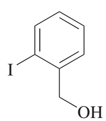
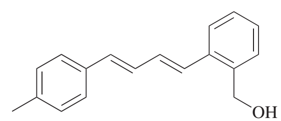
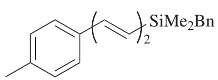
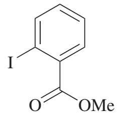
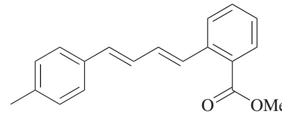
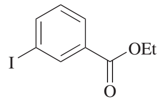
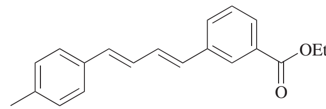
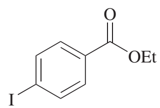
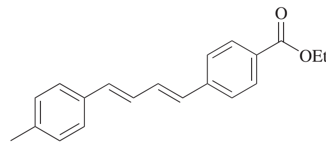
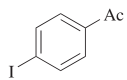
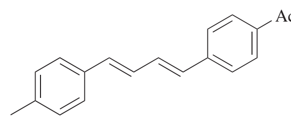
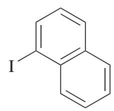
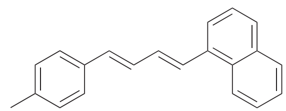
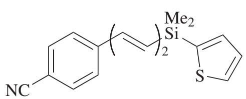
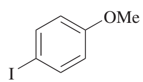
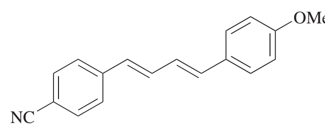
		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $TBAF$•$3H_2O$ (200%), THF, 35°		(72)	45
C_{11}					
		1. KOTMS (200%), 18-c-6 (200%), THF, rt, 30 min 2. Electrophile, $Pd_2(dba)_3$ (5%), 67°, 2 h		(62)	42
 110%		$Pd(dba)_2$ (3%), TBAF (200%), THF, rt, 30 min		(85)	225, 226
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(91)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(90)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 12 h		(89)	44

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{11}					
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(74)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(90)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(85)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(90)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 1 h		(92)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 2 h		(81)	44

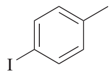
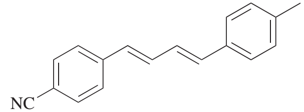
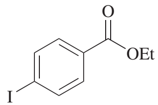
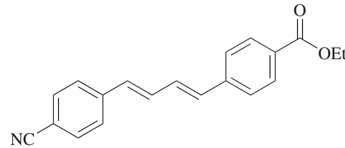
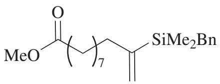
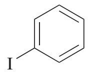
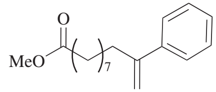
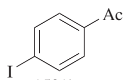
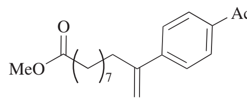
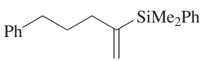
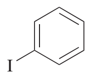
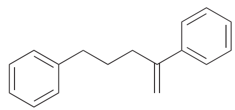
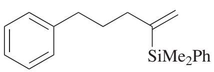
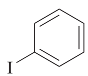
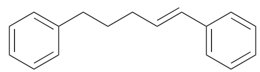
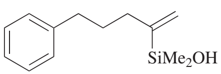
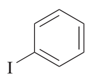
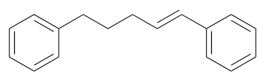
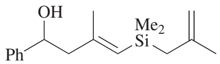
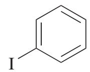
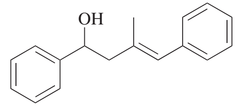
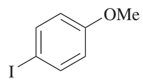
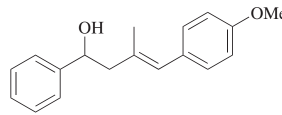
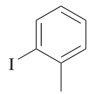
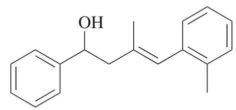
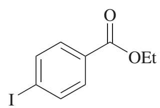
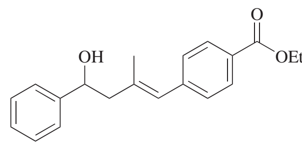
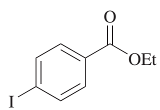
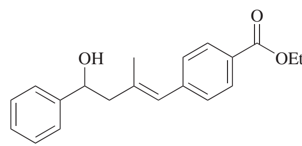
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 2 h	 (89)	44
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 2 h	 (90)	44
	 150%	1. TBAF (220%), 10 min, THF, 0° 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), rt, 4 h	 (97)	43
	 150%	1. TBAF (220%), 10 min, THF, 0° 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), rt, 4 h	 (89)	43
		1. KOTMS (200%), 18-c-6 (200%), THF, rt, 30 min 2. Electrophile, $Pd_2(dba)_3$ (5%), 67°, 2 h	 (86)	42
		$Pd_2(dba)_3$ (cat.), TBAF, *t*-BuOK, 18-c-6, THF, rt, 45 min	 (85) (*E*)/(*Z*) = 9:1	41
		$Pd_2(dba)_3$ (cat.), TBAF, THF, rt, 30 min	 (89) (*E*)/(*Z*) = 9:1	41

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{11}					
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(74)	157
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(70)	157
		1. TBAF (200%), $[allylPdCl]_2$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(11)	157
		1. TBAF (200%), $Pd_2(dba)_3$ (cat.), EtOH (600%), THF, rt, 30 min 2. Electrophile		(82)	157
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(82)	157

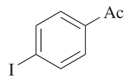
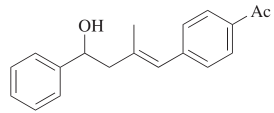
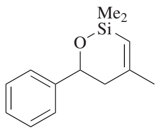
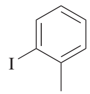
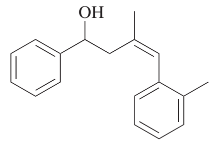
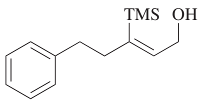
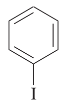
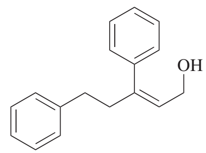
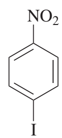
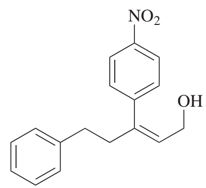
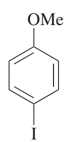
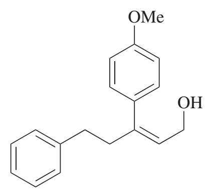
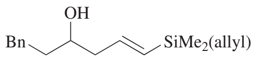
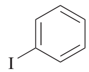
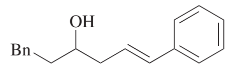
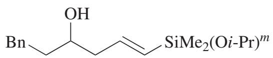
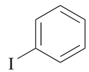
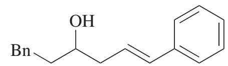
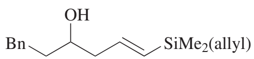
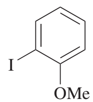
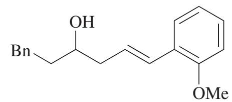
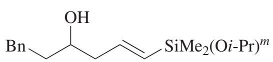
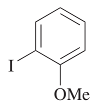
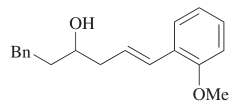
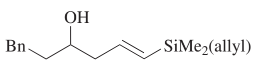
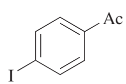
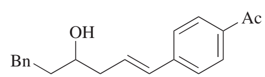
		1. TBAF (200%), Pd$_2$(dba)$_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(83)	157
		Pd(dba)$_2$ (3%), TBAF (200%), THF, rt, 45 min		(83)	225, 226
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, (Ph$_3$P)$_4$Pd (3%), 4 h 3. TBAF		(77)	127
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, (Ph$_3$P)$_4$Pd (3%), 4 h 3. TBAF		(63)	127
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, (Ph$_3$P)$_4$Pd (3%), 4 h 3. TBAF		(66)	127

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{12}					
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(97)	157
		$Pd_2(dba)_3$ (cat.), TBAF, THF, rt		(87)	222
		1. TBAF (200%), $[allylPdCl]_2$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(63)	157
		$[allylPdCl]_2$ (cat.), TBAF, THF, rt		(71)	222
		1. TBAF (200%), $Pd_2(dba)_3$ (5%), EtOH (600%), THF, rt, 30 min 2. Electrophile		(85)	157

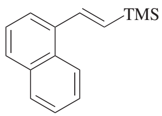
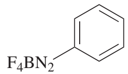
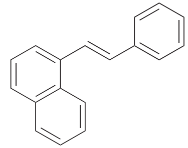
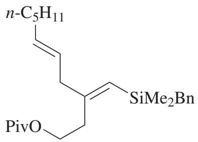
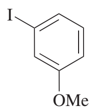
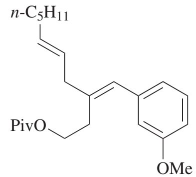
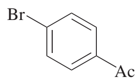
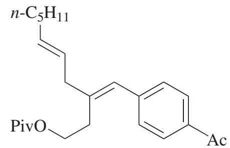
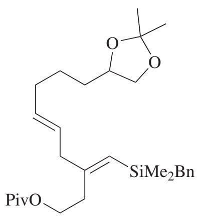
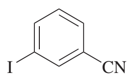
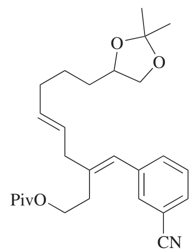
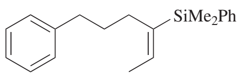
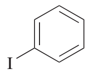
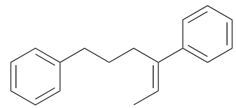
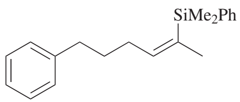
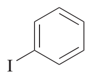
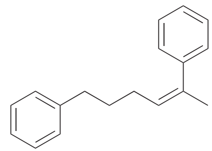
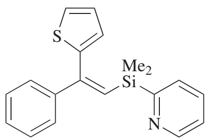
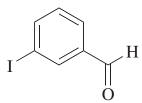
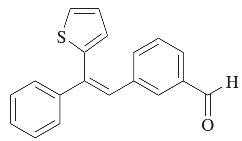
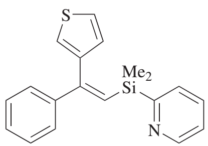
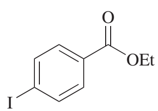
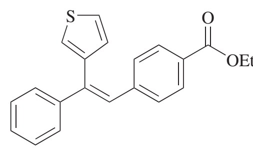
		1. BCl_3, CH_2Cl_2, 0° 2. $Pd(OAc)_2$ (6%), dioxane, rt, 24 h		(50)	124
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h		(60)	43
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h, 50°		(67)	43
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h, 50°		(92)	43

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{12}					
		1. KOTMS (200%), 18-c-6 (200%), THF, 67°, 30 min 2. Electrophile, $Pd_2(dba)_3$ (5%), 67°, 2 h		(76)	42
		1. KOTMS (200%), 18-c-6 (200%), THF, rt, 30 min 2. Electrophile, $Pd_2(dba)_3$ (5%), 67°, 2 h		(67)	42
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(80)	170
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(100)	170

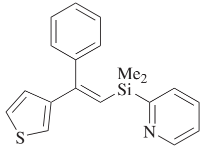
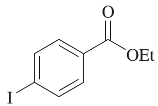
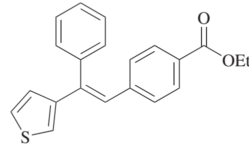
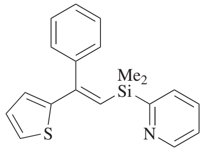
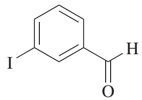
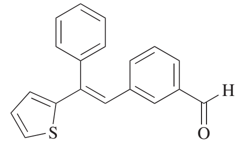
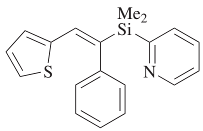
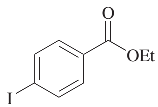
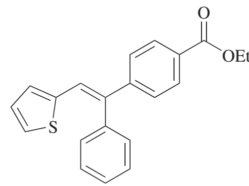
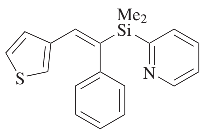
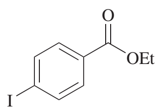
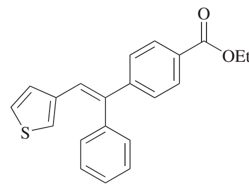
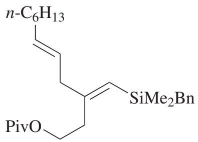
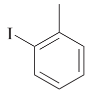
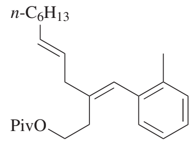
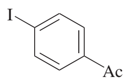
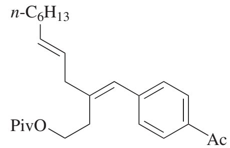
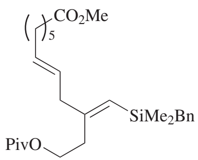
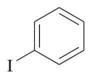
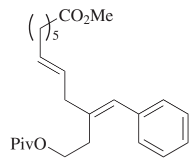
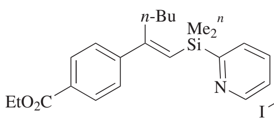
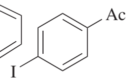
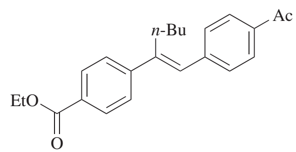
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(100)	170
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(84)	170
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(71)	170
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(71)	170

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{13}					
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h		(91)	43
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h		(91)	43
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 4 h		(88)	43
 150%		1. $Pd(OAc)_2$ (10%), (2-furyl)$_3$P (10%), Et_3N (160%), THF, 60° 2. Electrophile, TBAF (230%)		(71)	169, 170

C_{14}

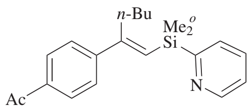
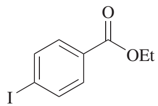
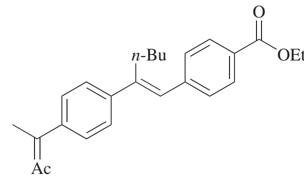
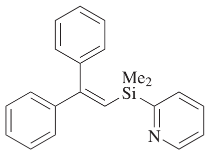
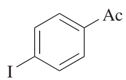
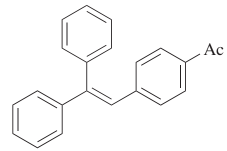
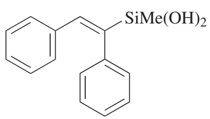
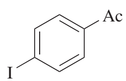
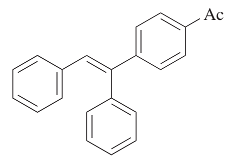
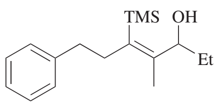
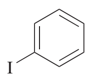
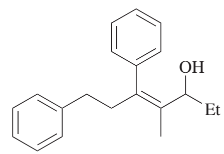
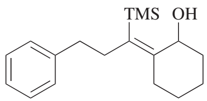
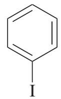
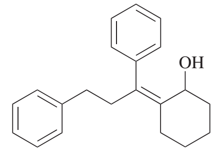
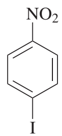
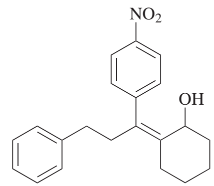
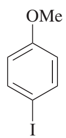
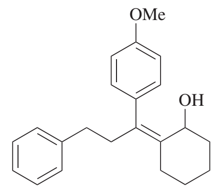
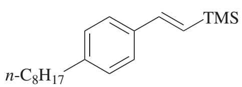
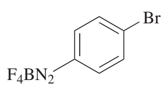
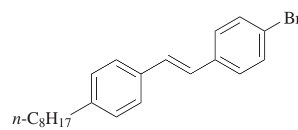
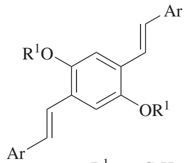
 150%		1. $Pd(OAc)_2$ (10%), $(2\text{-furyl})_3P$ (10%), Et_3N (160%), THF, 60° 2. Electrophile, TBAF (230%)		(79)	169, 170
 150%		$PdCl_2(PhCN)_2$ (5%), TBAF (150%), THF, 60°		(75)	170
 120%		$(Ph_3P)_4Pd$ (5%), Ag_2O (100%), THF, 60°, 24 h		(71)	37
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%), 4 h 3. TBAF		(77)	127

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

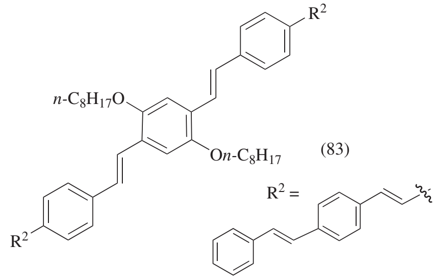
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%), 4 h 3. TBAF	 (78)	127
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%), 4 h 3. TBAF	 (67)	127
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%), 4 h 3. TBAF	 (60)	127
C_{16}				
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $Pd(OAc)_2$ (7%), dioxane, 24 h	 (62)	91

216%

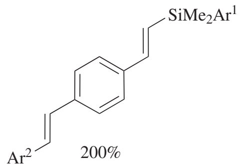


$R^1 = n\text{-}C_8H_{17}$
$Ar = 4\text{-}BrC_6H_4$

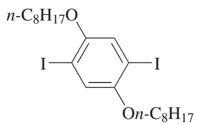
1. BCl_3, CH_2Cl_2, 0°
2. H_2O, Na_2CO_3
3. Electrophile, $(Ph_3P)_4Pd$ (20%), Na_2CO_3, toluene, MeOH, reflux



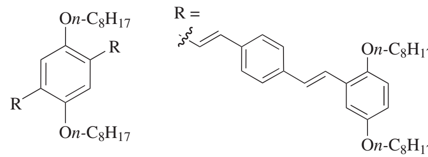
(83) 91



200%
$Ar^1 = 3,5\text{-}(CF)_3C_6H_3$
$Ar^2 = 2,5\text{-}(n\text{-}C_8H_{17}O)_2C_6H_3$

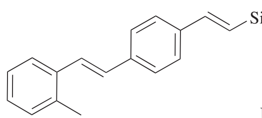


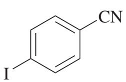
$[allylPdCl]_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt



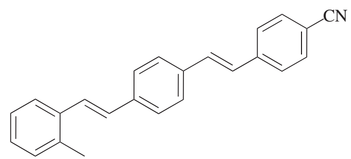
(>99) 166

C_{17}



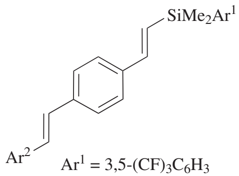
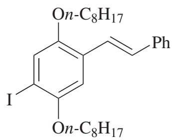
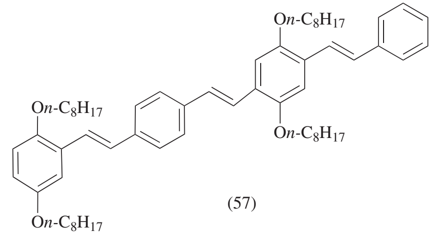
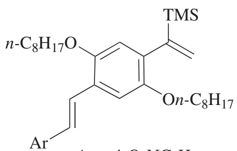
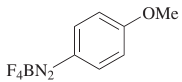
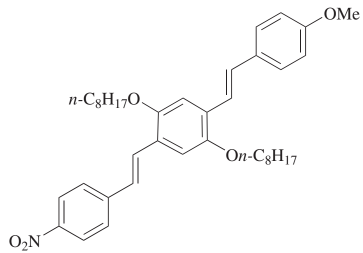
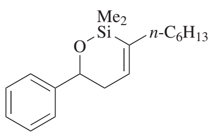
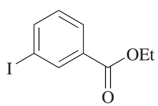
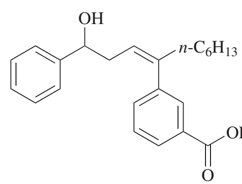


$[allylPdCl]_2$ (2.5%), TBAF (300%), rt

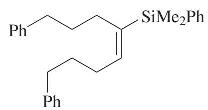


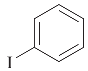
(76) 72

TABLE 3A. CROSS-COUPLING OF ALKENYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

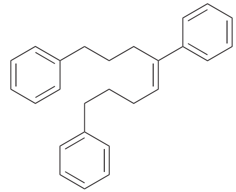
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}				
 Ar^1 = 3,5-$(CF)_3C_6H_3$ Ar^2 = 2,5-$(n\text{-}C_8H_{17}O)_2C_6H_3$		$[allylPdCl]_2$ (5%), TBAF•$3H_2O$ (100%), THF, rt	 (57)	166
 Ar = 4-$O_2NC_6H_4$	 400%	Pd(dba) (6%), MeCN, rt	 (93)	91
		$Pd(dba)_2$ (10%), TBAF (200%), THF, rt, 24 h	 (81)	225, 226

C_{20}



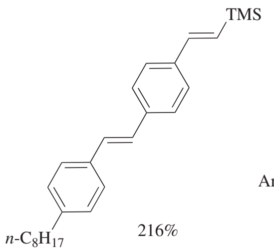


1. KOTMS (200%), 18-C-6 (200%), THF, rt, 30 min
2. Electrophile, $Pd_2(dba)_3$ (5%), 67°, 2 h

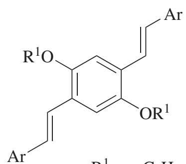


(82) 42

C_{24}

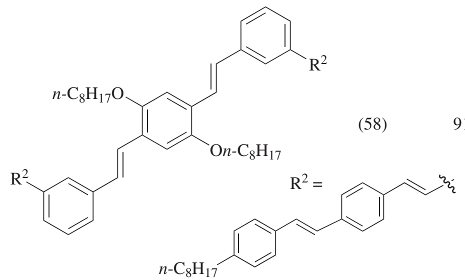


216%



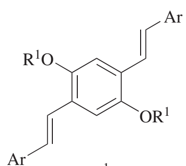
$R^1 = n\text{-}C_8H_{17}$
Ar = 3-BrC_6H_4

1. BCl_3, CH_2Cl_2, 0°
2. H_2O, Na_2CO_3
3. Electrophile, $(Ph_3P)_4Pd$ (20%), Na_2CO_3, toluene, MeOH, reflux



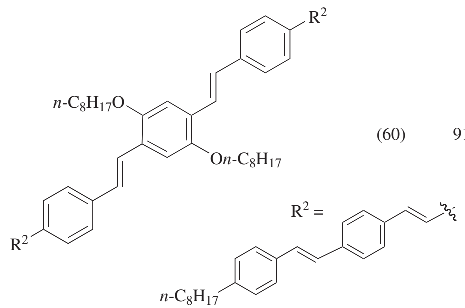
(58) 91

216%



$R^1 = n\text{-}C_8H_{17}$
Ar = 4-BrC_6H_4

1. BCl_3, CH_2Cl_2, 0°
2. H_2O, Na_2CO_3
3. Electrophile, $(Ph_3P)_4Pd$ (20%), Na_2CO_3, toluene, MeOH, reflux



(60) 91

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.

[a] The starting silane was generated in situ by reaction of pent-4-yn-1-ol with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[b] The starting silane was generated in situ by reaction of 5-(allyloxy)pent-1-yne with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of *t*-Bu_3-Pt(DVDS).

[c] The starting silane was generated in situ by treating pent-3-yn-1-ol with tetramethyldisilazane followed by catalytic amounts of *t*-Bu_3-PPt(DVDS).

[d] The starting silane was generated in situ by the reaction of allyl(isopropoxy)dimethylsilane with *s*-BuLi (110%) and acetone (110%) at –78°.

[e] The starting silane was generated in situ by treating 1-heptyne with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[f] The starting silane was generated in situ by treating *tert*-butyl 2-((4*R*,6*S*)-6-ethynyl-2,2-dimethyl-1,3-dioxan-4-yl)acetate with dimethylchlorosilane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[g] The starting silane was generated in situ by treating phenylacetylene with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[h] The starting silane was generated in situ by treating oct-3-yn-1-ol with tetramethyldisilazane followed by catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[i] The starting silane was generated in situ by the reaction of allyl(isopropoxy)dimethylsilane with cyclohexanone at –78° in the presence of *s*-BuLi followed by quenching with acetic acid.

[j] The starting silane was generated in situ by the reaction of isopropoxy(dimethyl)[(*Z*)-2-(tributylstannyl)vinyl]silane with ethyl 4-iodobenzoate under palladium catalysis.

[k] The starting silane was generated in situ by the reaction of allyl(isopropoxy)dimethylsilane with benzaldehyde at –78° in the presence of *s*-BuLi followed by quenching with acetic acid.

[l] The starting silane was generated in situ by treating 2-phenylbut-3-yn-2-ol with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[m] The starting silane was generated in situ by the reaction of allyl(isopropoxy)dimethylsilane with 3-phenylpropanal at –78° in the presence of *s*-BuLi followed by quenching with acetic acid.

[n] The starting silane was generated in situ by the reaction of (*E*)-(1-hexenyl)dimethyl(2-pyridyl)silane with ethyl 4-iodobenzoate, $Pd(OAc)_2$, (2-furyl)$_3$P, and Et_3N.

[o] The starting silane was generated in situ by the reaction of (*E*)-(1-hexenyl)dimethyl(2-pyridyl)silane with 4-iodoacetophenone, $Pd(OAc)_2$, (2-furyl)$_3$P, and Et_3N.

TABLE 3B. CROSS-COUPLING OF ALKENYLSILANES WITH HETEROARYL ELECTROPHILES

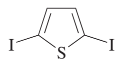
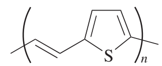
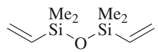
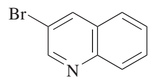
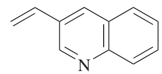
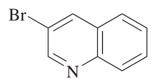
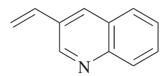
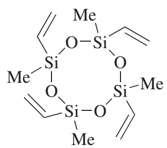
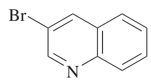
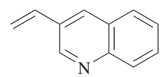
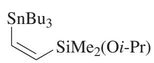
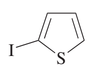
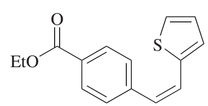
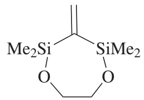
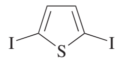
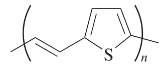
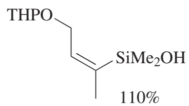
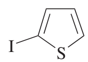
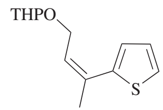
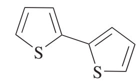
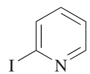
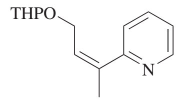
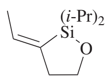
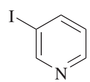
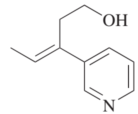
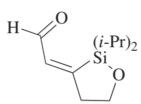
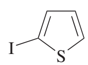
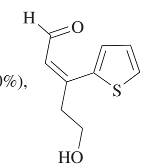
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 90%	1. $Ru(H)Cl(CO)(PPh_3)_3$ (2%), CuCl (2%), dioxane, 110° 2. Electrophile, Pd_2dba_3 (1%), TBAF (240%), dioxane, 80°, 24 h	 (90)	104
 110%		$Pd(dba)_2$ (5%), $Ph_3P(O)$ (5%), KOTMS (350%), THF, reflux, 3 h	 (91)	262
130%		JohnPhos (5%), $[allylPdCl]_2$ (2.5%), $KOSiEt_3$ (300%), DMF, rt, 2 h	 (79)	262
 50%		JohnPhos (10%), $PdBr_2$ (5%), TBAF (200%), THF, 50°, 3 h	 (89)	318
		1. Ethyl 4-iodobenzoate, $PhCH_2PdCl(PPh_3)_2$, CuI, DMF, 50° 2. 2-Iodothiophene, TBAF, 50°	 (61)	128

TABLE 3B. CROSS-COUPLING OF ALKENYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 90%	$Pd_2(dba)_3$ (1%), TBAF (240%), dioxane, 80°, 24 h	 (97)	104
C_4				
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 300 min	 (80) +  (20)	79
110%		$Pd(dba)_2$ (6%), TBAF (200%), THF, 35°, 41 h	 (66)	79
C_5				
 110%		1. TBAF (200%) 2. $Pd(dba)_2$ (5%), THF, 45°, 45 h	 (73)	79
 130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%), $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 3 h	 (78)	81

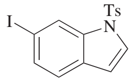
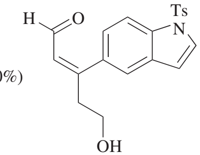
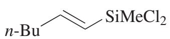
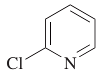
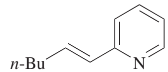
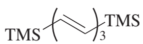
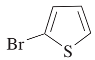
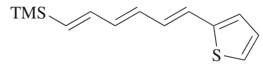
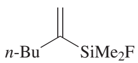
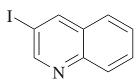
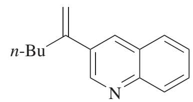
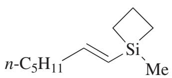
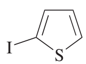
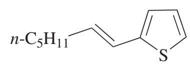
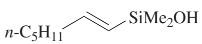
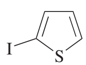
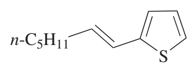
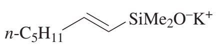
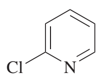
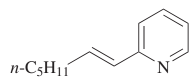
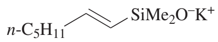
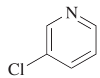
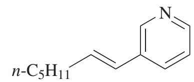
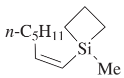
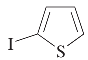
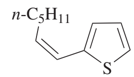
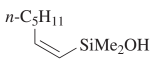
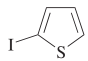
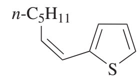
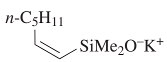
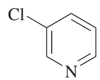
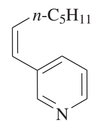
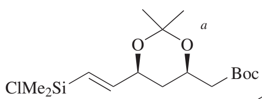
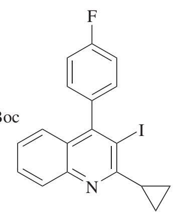
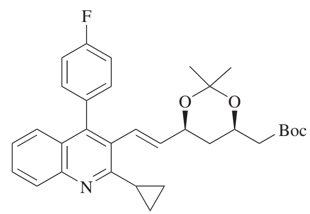
130%		$[allylPdCl]_2$ (5%), CuI (10%), KF $2H_2O$ (200%) $[–MeSi(H)O–]_{3–5}$ (2.5%), DMF, rt, 2 h	 (88)	81
C_6				
 120%		$(i\text{-}Pr_3P)_2PdCl_2$ (2.5%), NaOH (600%), C_6H_6, 80°, 12 h	 (79)	185
		1. BCl_3, CH_2Cl_2, 0° 2. Electrophile, $(Ph_3P)_4Pd$ (cat.), NaOH (2 M), benzene, reflux	 (38)	125
 150%		$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 60°, 44 h	 (64)	172
C_7				
 120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 180 min	 (89) $(E)/(Z)$ = 99.0:1.0	38
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 180 min	 (83) $(E)/(Z)$ = 95.7:4.3	31
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 3 h	 (87) $(E)/(Z)$ = 99.6:0.4	80

TABLE 3B. CROSS-COUPLING OF ALKENYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1.5 h		(85) (*E*)/(*Z*) = 99.8:0.2	80
 120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 180 min		(85) (*Z*)/(*E*) = 97.8:2.2	38
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 180 min		(81) (*Z*)/(*E*) = 97.5:2.5	31
 150%		SPhos (5%), $[allylPdCl]_2$ (2.5%), THF, 60°, 1.5 h		(91) (*Z*/(*E*) = 99.3:0.7	80
 [a]		1. *t*-Bu_3Pt(DVDS) (0.5%), $Me_2SiCl(H)$ (120%), rt, 1 h 2. Electrophile, $[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 0.5 h		(83) (*E*)/(*Z*) = 96:4	177

C_8

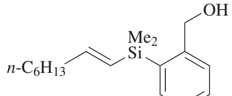
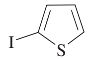
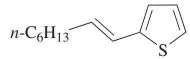
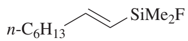
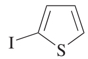
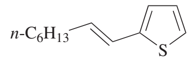
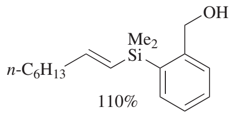
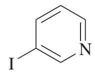
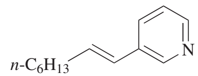
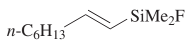
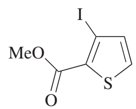
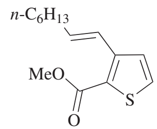
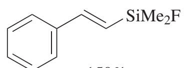
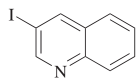
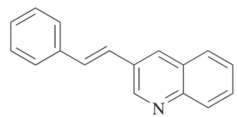
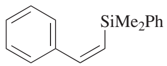
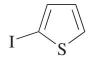
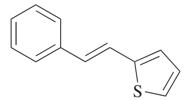
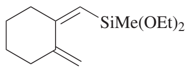
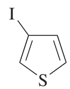
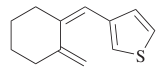
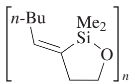
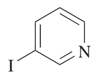
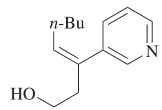
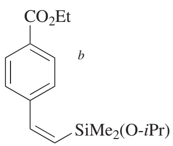
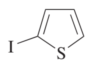
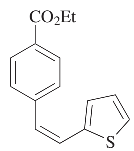
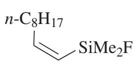
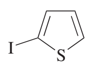
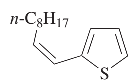
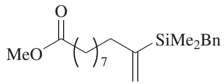
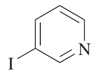
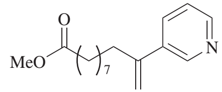
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 23 h		(99)	150, 151
 150%		[allylPdCl]$_2$ (2.5%), TBAF (150%), THF, 60°, 12 h		(78)	172
 110%		$PdCl_2$ (1%), (2-furyl)$_3$P (2%), K_2CO_3 (220%), DMSO, 35°, 23 h		(80)	150, 151
 150%		[allylPdCl]$_2$ (2.5%), TBAF (150%), THF, 60°, 36 h		(74)	172
 150%		[allylPdCl]$_2$ (2.5%), TBAF (150%), THF, 60°, 18 h		(84)	172

TABLE 3B. CROSS-COUPLING OF ALKENYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

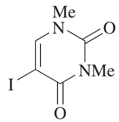
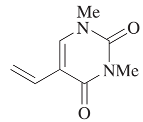
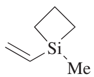
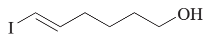
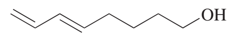
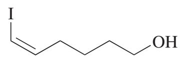
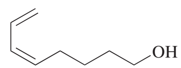
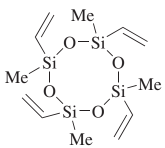
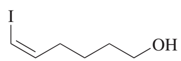
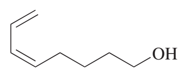
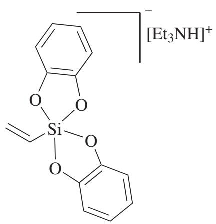
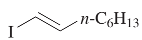
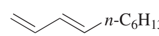
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$(Ph_3P)_4Pd$ (2.5%), TBAF (150%), Et_3N (100%), THF, 65°, 112 h	 (31)	162
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 7 h	 (77) (*Z*)/(*E*) = 91:9	26
		$Pd(dba)_2$ (5%), TBAF (1000%), 45°, 7 d	 (59)	188
C_9				
 *b* 111%		PdCl(PPh_3)(Bn) (5%), CuI (10%), TBAF (278%), DMF, 50°, 8 h	 (61)	128
C_{10}				
 150%		$[allylPdCl]_2$ (2.5%), TASF (50%), DMF, 60°, 5 h	 (62)	172

C_{11}					
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), 50°, 4 h		(78)	43

[a] The starting silane was generated in situ by treating *tert*-butyl 2-((4*R*,6*S*)-6-ethynyl-2,2-dimethyl-1,3-dioxan-4-yl)acetate with dimethylchlorosilane in the presence of catalytic amounts of *t*-Bu_3P-Pt(DVDS).

[b] The starting silane was generated in situ by reaction of isopropoxy(dimethyl)[(*Z*)-2-(tributylstannyl)vinyl]silane with ethyl 4-iodobenzoate under palladium catalysis.

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
		$[allylPdCl]_2$ (2.5%), TBAF (400%), THF, 60°, 14 h		(82)	88
 120%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 1 h		(46) (*E*)/(*Z*) = 100:0	40
120%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 1 h		(48) (*Z*)/(*E*) = 98:2	40
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 180 min		(52) (*Z*)/(*E*) = 94:6	267
		$PdCl_2PhCN_2$ (5%), $(EtO)_3P$ (10%), dioxane, reflux, 60 h		(29)	22

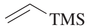
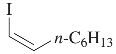
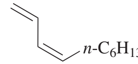
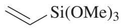
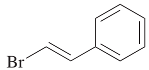
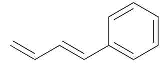
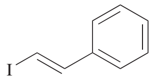
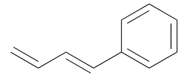
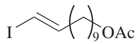
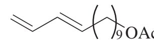
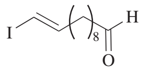
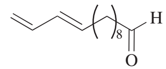
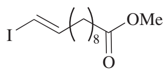
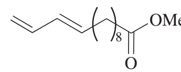
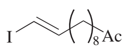
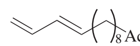
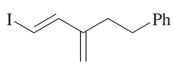
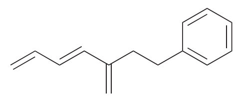
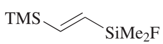
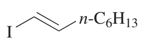
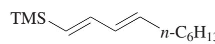
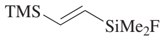
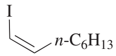
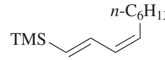
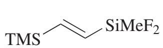
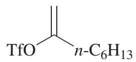
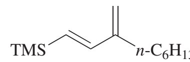
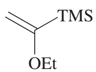
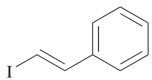
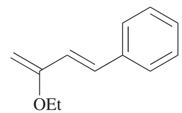
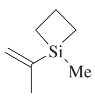
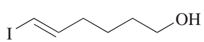
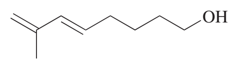
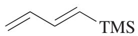
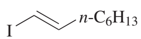
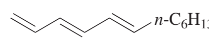
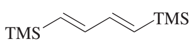
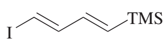
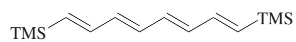
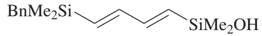
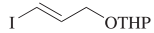
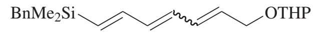
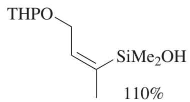
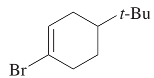
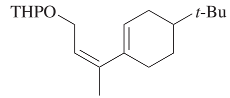
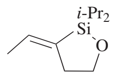
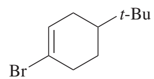
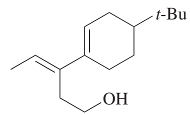
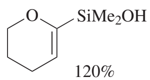
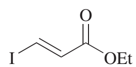
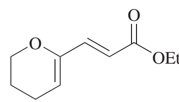
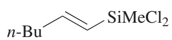
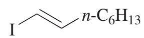
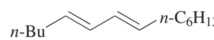
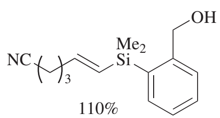
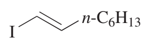
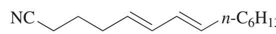
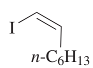
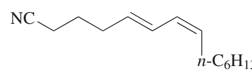
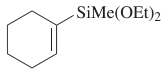
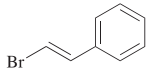
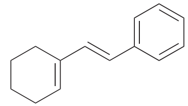
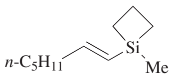
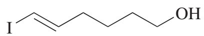
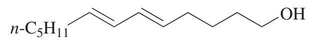
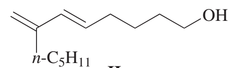
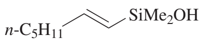
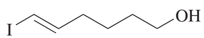
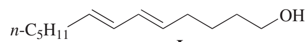
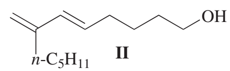
 130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(76)	23
 200%		Pd cat. **5** (0.5%), NaOH (250%), TBAB (100%), H_2O, MW, 15 min		(81)	257
 130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(93)	23
130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(70)	23
130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(52)	23
130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(88)	23
130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(67)	23
130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°		(85)	23
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 15 h		(70)	25

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 12 h	 (55)	25
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 5 h	 (90)	181
 130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°	 (181)	23
C_3				
 120%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 12 h	 (71) (*E*)/(*Z*) = 100:0	40
C_4				
		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°	 (78)	23
		1. BCl_3, CH_2Cl_2, 0° 2. Na_2CO_3 (2 M) 3. Electrophile, $(Ph_3P)_4Pd$ (cat.), Na_2CO_3 (2 M), MeOH, toluene, reflux	 (70)	90, 125

 150%		$Pd_2(dba)_3$•$CHCl_3$ (5%), NaH (140%), THF, rt, 6 h		(77) dr = 3:1	216
 110%		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 45°, 48 h		(31)	79
C_5					
 110%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), THF, 45°, 47 h		(45)	224
 120%		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%), rt, THF, 2 h		(81)	171
C_6					
 120%		$Pd(OAc)_2$ (2.5%), NaOH (600%), THF, 60°, 12 h		(58)	185
 110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (210%), **L4** (5%), DMSO, 35°, 3 h		(73)	151
110%		$PdCl_2$ (1%), $(2\text{-furyl})_3P$ (2%), K_2CO_3 (210%), **L4** (5%), DMSO, 35°, 3 h		(73)	151

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 16 h	 (63)	26
C_7				
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 90 min	 **I** +  **II** **I** + **II** (95), **I**:**II** = 90:10 **I** (*E*,*E*)/(*E*,*Z*) = 98.4:1.6	38
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 90 min	 **I** +  **II** **I** + **II** (95), **I**:**II** = 86:14 **I** (*E*,*E*)/(*E*,*Z*) = 95.8:4.2	31

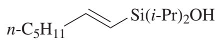
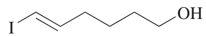
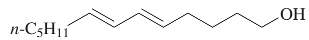
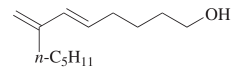
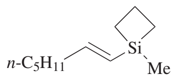
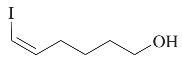
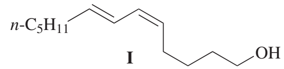
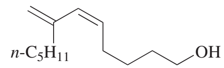
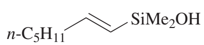
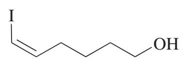
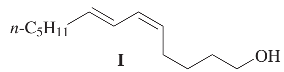
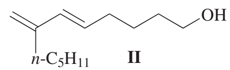
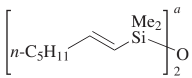
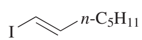
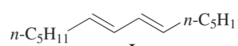
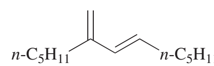
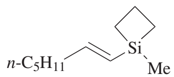
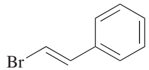
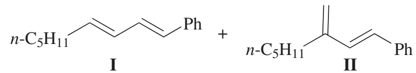
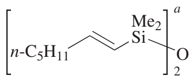
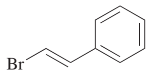
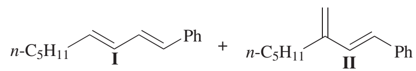
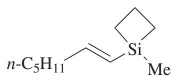
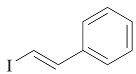
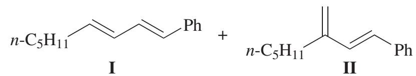
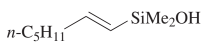
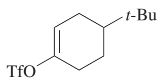
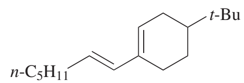
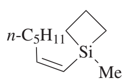
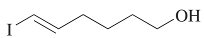
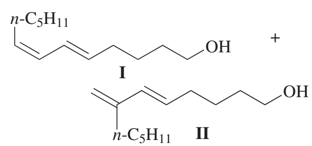
C_7				
 110%		Pd(dba)$_2$ (5%), TBAF (200%), THF, rt, 90 min	 **I** +  **II** **I** + **II** (87), **I**:**II** = 96:4 **I** (*E*,*E*)/(*E*,*Z*) = 97.8:2.2	31
 110%		Pd(dba)$_2$ (5%), TBAF (200%), THF, rt, 90 min	 **I** +  **II** **I** + **II** (70), **I**:**II** = 99:1 **I** (*E*,*Z*)/((*Z*,*Z*) + (*E*,*E*)) = 97.0:3.0	38
 110%		Pd(dba)$_2$ (5%), TBAF (200%), THF, rt, 90 min	 **I** +  **II** **I** + **II** (73), **I**:**II** = 99:1 **I** (*Z*,*E*)/(*Z*,*Z*) = 94.1:5.9	31
 [a] 130%		Pd(dba)$_2$ (5%), TBAF (200%), THF, rt, 16 h	 **I** +  **II** **I** + **II** (67) (*E*,*E*)/((*E*,*Z*) + **II**) = 91.4:8.6	261

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 120%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 60 min	 I + II (80), I:II = 98:2; I (*E*,*E*)/(*E*,Z) = 98.4:1.6	38
 130%		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, rt, 14 h	 I + II (70) (*E*,*E*)/(*E*,Z)/II = 92.0:3.2:4.8	261
 110%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 I + II (73), I:II = 96:4; I (*E*,*E*)/(*E*,Z) = 98.0:2.0	38
 110%		JohnPhos (10%), $PdBr_2$ (5%), TBAF•$3H_2O$ (200%), dioxane, 50°	 (62) (*E*)/(*Z*) = 98.7:1.3	202
 120%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 90 min	 I + II (74), I:II = 85:15; I (*E*,*Z*)/((Z,Z) + (*E*,*E*)) = 97.0:3.0	38

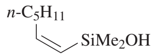
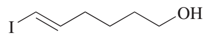
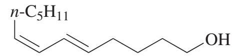
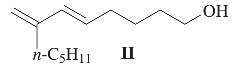
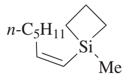
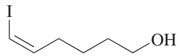
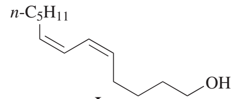
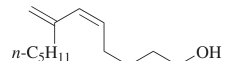
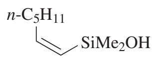
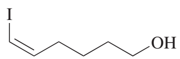
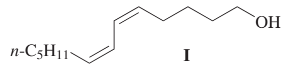
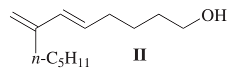
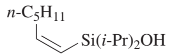
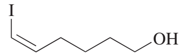
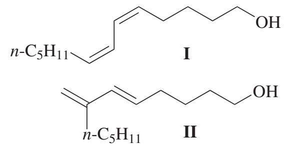
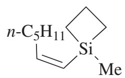
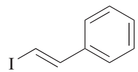
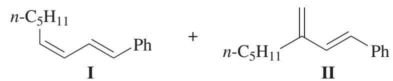
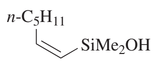
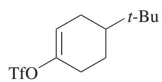
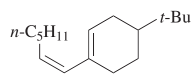
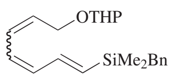
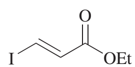
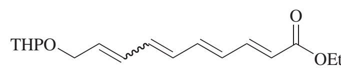
 110%		$Pd(dba)_2$ (5%), TBAF (200%), THF, rt, 90 min	 I +  II **I** + **II** (72), **I**:**II** = 91:9 (*E*,*Z*)/((*Z*,*Z*) + (*E*,*E*)) = 95.4:4.6	31
 120%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 300 min	 I +  II **I** + **II** (65), **I**:**II** = 99:1 **I** (*Z*,*Z*)/other isomers = 94.8:5.2	38
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, rt, 300 min	 I +  II **I** + **II** (64), **I**:**II** = 99:1 **I** (*Z*,*Z*)/other isomers = 87.8:12.2	31

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
 150%		$[allylPdCl]_2$ (2.5%), TBAF (300%), THF, rt, 300 min	 **I** + **II** (68), **I**:**II** = 93.2:6.8 **I** (*Z*,*Z*)/other isomers = 92.4:7.6	31
 120%		$Pd(dba)_2$ (5%), TBAF (300%), THF, rt, 10 min	 **I** + **II** (75), **I**:**II** = 98:2 **I** (*E*,*Z*)/((*Z*,*Z*) + (*E*,*E*)) = 97.2:2.8	38
 110%		JohnPhos (10%), $PdBr_2$ (5%), TBAF•$6H_2O$ (200%), dioxane, 50°, 25 h	 (65) (*Z*)/(*E*) = 96.6:3.4	202
		$Pd(dba)_2$ (cat.), TBAF	 (79) dr = 5:1	216

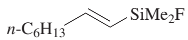
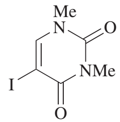
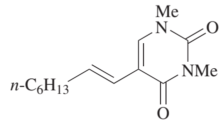
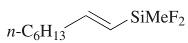
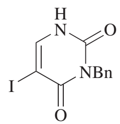
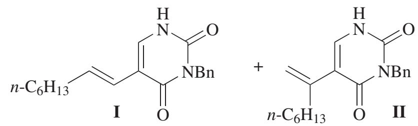
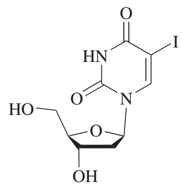
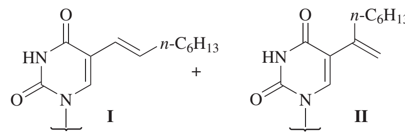
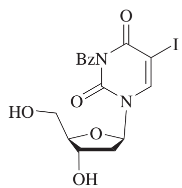
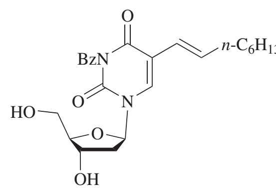
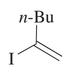
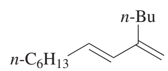
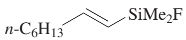
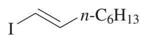
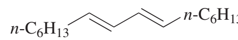
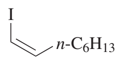
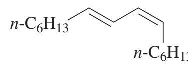
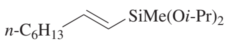
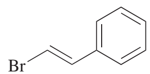
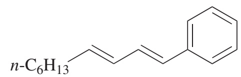
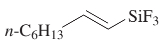
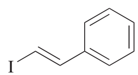
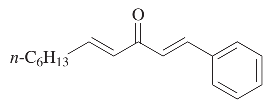
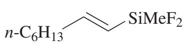
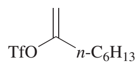
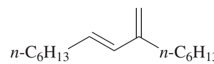
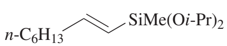
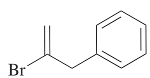
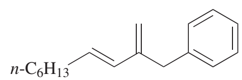
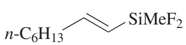
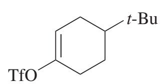
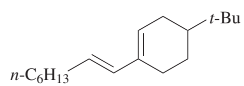
C_8				
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 14 h	 (70)	88
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 44 h	 **I** + **II** (53), **I**:**II** = 2:1	88
		$[allylPdCl]_2$ (2.5%), TBAF (200%), DMF, 60°	 **I** + **II** (74), **I**:**II** = 2:1	88
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°	 (60)	88
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 22 h	 (69)	25

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 16 h		(83)	25
		$[allylPdCl]_2$ (2.5%), TASF (150%), THF, 21 h		(89)	25
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 16 h		(71)	26
 150%		$[allylPdCl]_2$ (2.5%), TBAF (200%), CO (1 atm), THF, 50°, 20 h		(45)	179
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 4 h		(82)	181
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 12 h		(31)	26
 120%		$(Ph_3P)_4Pd$ (cat.), TBAF (120%), THF, 50°, 0.5 h		(99)	181

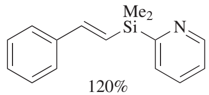
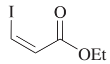
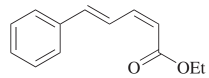
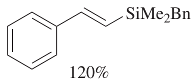
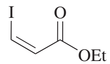
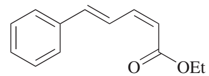
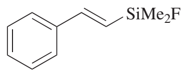
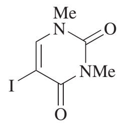
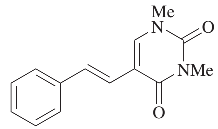
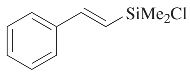
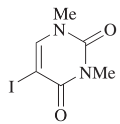
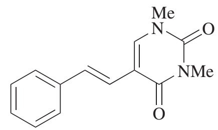
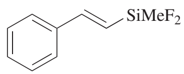
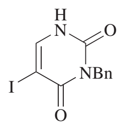
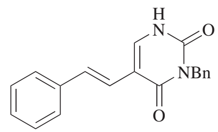
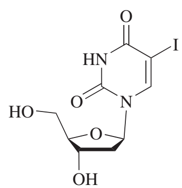
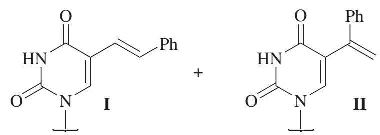
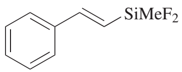
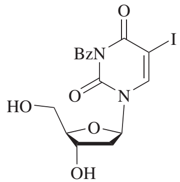
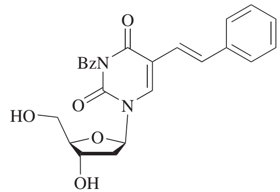
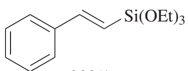
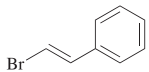
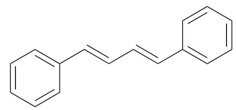
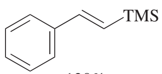
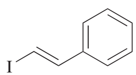
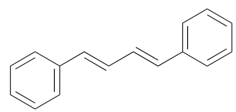
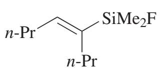
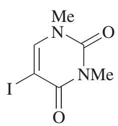
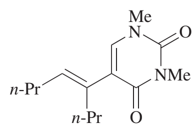
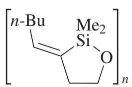
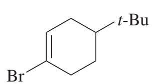
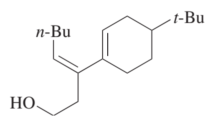
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(91)	169
 120%		$PdCl_2(PhCN)_2$ (5%), TBAF (100%), THF, 60°		(91)	169
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 16 h		(69)	88
		$[allylPdCl]_2$ (2.5%), TBAF (400%), THF, 60°, 14 h		(70)	88
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 48 h		(58)	88
		$[allylPdCl]_2$ (2.5%), TBAF (200%), DMF, 60°	 **I** + **II** (79), **I**:**II** = 5:1		88

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°	 (64)	88
 200%		Pd cat. **5** (0.5%), NaOH (250%), TBAB (100%), H_2O, 120° (MW), 20 min	 (81) (*E*)/(*Z*) = 2:1	257
 130%		$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TASF (130%), THF, 50°	 (32)	23
		$[allylPdCl]_2$ (2.5%), TBAF (200%), THF, 60°, 11 h	 (63)	88
		$[allylPdCl]_2$ (3.7%), TBAF (100%), 45°, 3 d	 (32)	198

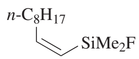
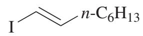
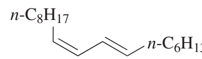
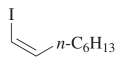
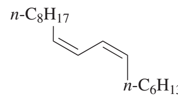
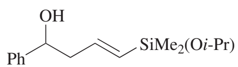
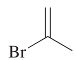
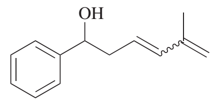
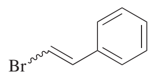
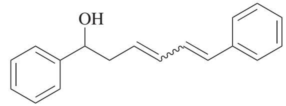
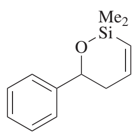
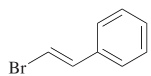
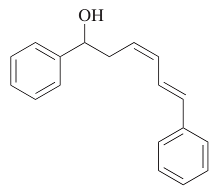
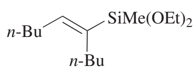
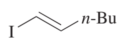
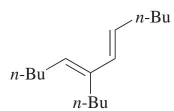
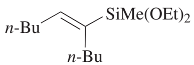
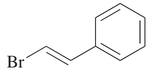
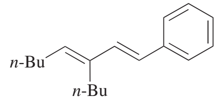
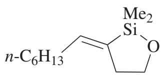
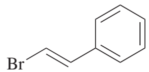
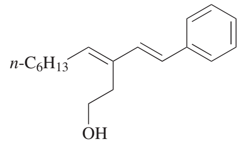
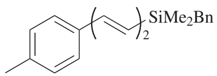
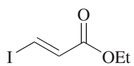
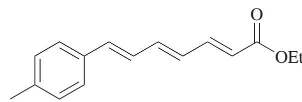
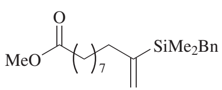
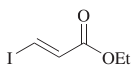
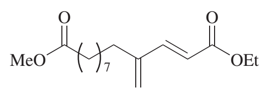
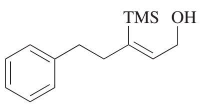
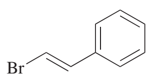
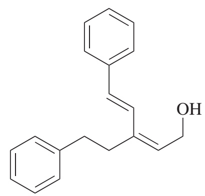
C_{10}					
		$(Ph_3P)_4Pd$ (5%), TASF (150%), DMF, 14 h		(84)	25
		$(Ph_3P)_4Pd$ (5%), TASF (150%), DMF, 19 h		(74)	25
		$[allylPdCl]_2$ (cat.), TBAF (200%), THF, 50°, 24 h		(38)	222
		$[allylPdCl]_2$ (cat.), TBAF (200%), THF, 50°, 2 h		(66)	222
		1. TBAF (200%) 2. $[allylPdCl]_2$ (2.5%)		(78)	226
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 6 h		(45)	26

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°, 16 h	 (73)	26
	 110%	$[allylPdCl]_2$ (2.5%), $(EtO)_3P$ (5%), TBAF (150%), THF, 50°	 (43)	26
C_{11}				
		$Pd(dba)_2$ (2.5%), TBAF (200%), THF, rt, 4 h	 (72)	44
	 150%	1. TBAF (220%), THF, 0°, 10 min 2. $Pd_2(dba)_3$•$CHCl_3$ (2.5%), rt, 4 h	 (65)	43
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%), 4 h 3. TBAF	 (63)	127

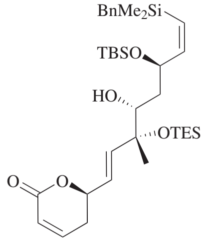
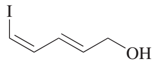
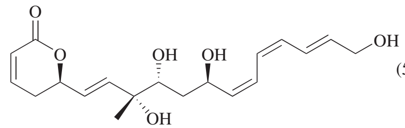
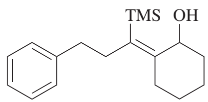
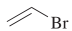
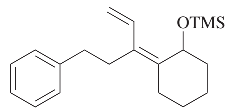
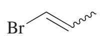
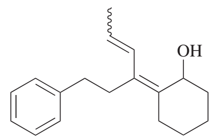
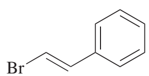
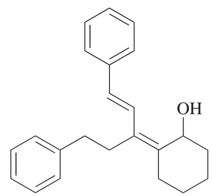
C_{14}					
		$Pd_2(dba)_3$•$CHCl_3$ (5%), TBAF (400%), THF, 0° to rt		(54)	324
C_{15}					
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%)		(71)	127
	 120% *E*/*Z* = 75:25	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%)		(61) (*E*)/(*Z*) = 70:30	127
	 120%	1. *t*-BuOCu (120%), DMF, rt 2. Electrophile, $(Ph_3P)_4Pd$ (3%) 3. TBAF		(72)	127

TABLE 3C. CROSS-COUPLING OF ALKENYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.

[a] The starting silane was generated in situ by treating 1-heptyne with 1,1,3,3-tetramethyldisiloxane in the presence of catalytic amounts of t-Bu_3P-Pt(DVDS).

TABLE 3D. CROSS-COUPLING OF ALKENYLSILANES WITH ALLYL ELECTROPHILES

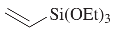
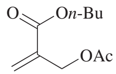
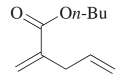
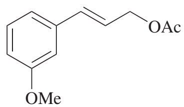
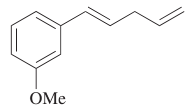
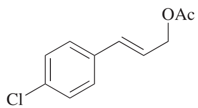
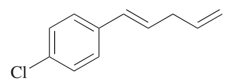
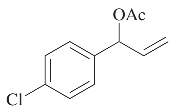
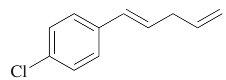
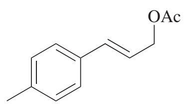
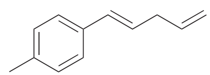
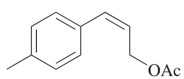
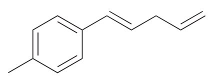
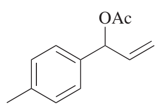
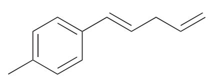
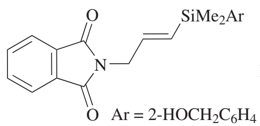
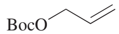
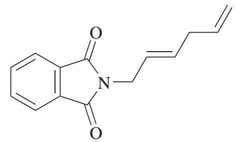
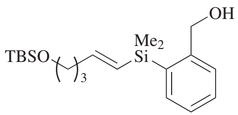
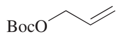
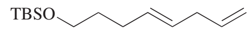
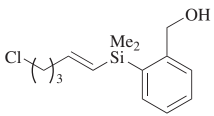
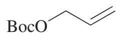
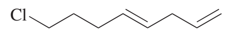
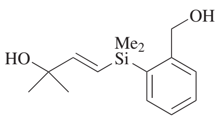
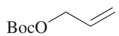
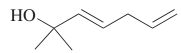
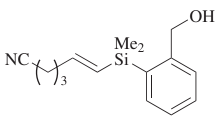
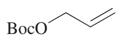
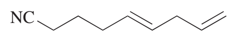
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 7 h		(85)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 8 h		(75)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 7 h		(80)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 7 h		(80)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 8 h		(78)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 8 h		(78)	254
		$PdCl_2$ (2%), TBAB (25%), TBAF (120%), THF, reflux, 8 h		(78)	254

TABLE 3D. CROSS-COUPLING OF ALKENYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_3					
		$Pd_2(dba)_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 3 h		(85)	152
C_5					
		$Pd_2(dba)_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 2 h		(72)	152
		$Pd_2(dba)_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 2 h		(74)	152
		$Pd_2(dba)_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 4 h		(53)	152
C_6					
		$Pd_2(dba)_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 4 h		(85)	152

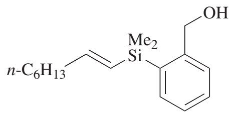
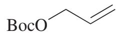
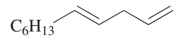
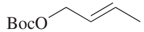
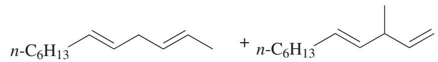
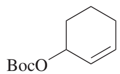
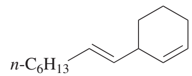
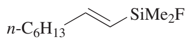
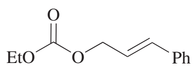
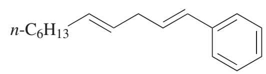
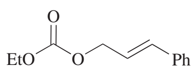
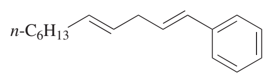
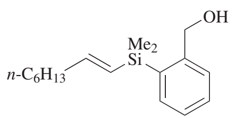
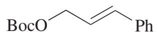
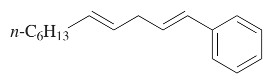
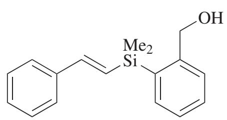
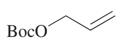
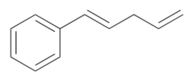
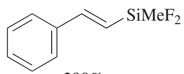
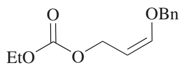
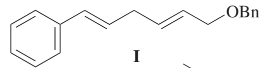
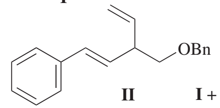
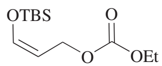
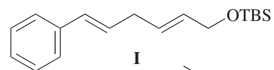
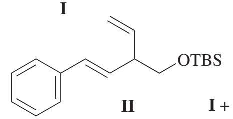
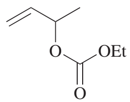
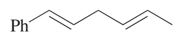
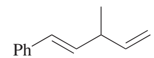
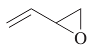
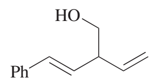
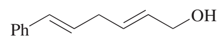
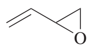
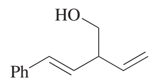
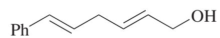
C_8					
		$Pd_2(dba)_3$ (0.5%), $(2\text{-furyl})_3P$ (2%), THF, 50°, 2 h		(85)	152
		$Pd_2(dba)_3$ (0.5%), $(2\text{-furyl})_3P$ (2%), THF, 50°, 3 h	 **I** + **II** **I** + **II** (68), **I**:**II** = 73:27		152
		$Pd_2(dba)_3$ (0.5%), $(2\text{-furyl})_3P$ (2%), THF, 50°, 3 h		(93)	152
 200%		$Pd(OAc)_2$ (5%), Ph_3P (5%), DMF, 60°, 24 h		(72)	175, 176
200%		$Pd(OAc)_2$ (5%), Ph_3P (5%), DMF, 60°, 28 h		(73)	175, 176
		$Pd_2(dba)_3$ (0.5%), $(2\text{-furyl})_3P$ (2%), THF, 50°, 3 h		(93)	152
		$Pd_2(dba)_3$ (0.5%), $(2\text{-furyl})_3P$ (2%), THF, 50°, 2 h		(91)	152

TABLE 3D. CROSS-COUPLING OF ALKENYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 200%		$Pd(OAc)_2$ (5%), Ph_3P (5%), DMF, 90°, 1.5 h	 **I** +  **II** **I** + **II** (80), **I**:**II** = 2.5:1	175, 176
		$Pd(OAc)_2$ (5%), Ph_3P (5%), DMF, 90°, 4 h	 **I** +  **II** **I** + **II** (69), **I**:**II** = 2:1	175, 176
200%		$Pd(OAc)_2$ (5%), Ph_3P (5%), DMF, 90°, 1.5 h	 +  **I** **I** + **II** (76), **I**:**II** = 4.4:1 **II**	175, 176
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $(2\text{-MePh})_3P$ (10%), benzene, 40°	 +  **I** **I** + **II** (41), **I**:**II** = 1:4.8 **II**	175
200%		$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OCH_2)_3CEt$ (10%), benzene, 40°	 +  **I** **I** + **II** (59), **I**:**II** = 1:5.9 **II**	175

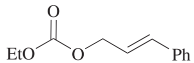
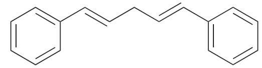
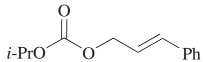
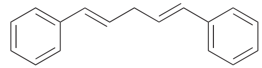
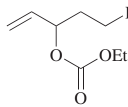
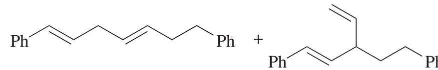
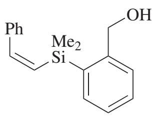
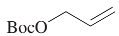
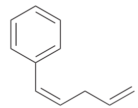
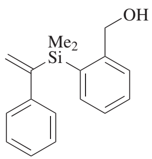
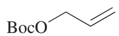
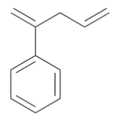
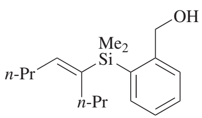
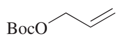
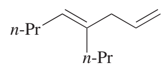
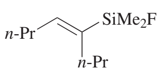
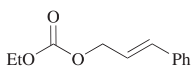
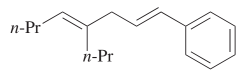
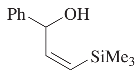
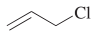
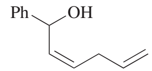
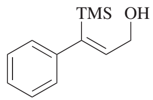
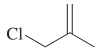
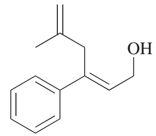
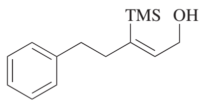
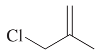
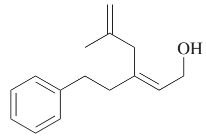
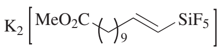
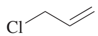
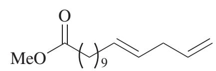
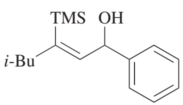
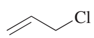
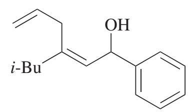
200%		Pd(OAc)$_2$ (5%), Ph_3P (5%), DMF, 60°, 2 h		(91)	175
200%		Pd(OAc)$_2$ (5%), Ph_3P (5%), DMF, 60°, 1 h		(94)	175
200%		Pd(OAc)$_2$ (5%), Ph_3P (5%), DMF, 90°, 1 h	 **I** **I** + **II** (90), **I**:**II** = 3.5:1 **II**		175, 176
		Pd$_2$(dba)$_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 2 h		(92)	152
		Pd$_2$(dba)$_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 3 h		(81)	152
		Pd$_2$(dba)$_3$ (0.5%), (2-furyl)$_3$P (2%), THF, 50°, 24 h		(78)	152
 200%		Pd(OAc)$_2$ (5%), Ph_3P (5%), DMF, 60°, 48 h		(40) 31% rsm	175

TABLE 3D. CROSS-COUPLING OF ALKENYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_9					
 (*Z*)/(*E*) = 95:5	 120%	1. CuO*t*-Bu (100%), DMF, rt 2. TBAF (100%)		(67)	128
	 120%	1. *t*-BuOCu (120%), DMF, rt, 15 h 2. TBAF		(74)	126, 127
C_{11}					
	 120%	1. *t*-BuOCu (120%), DMF, rt, 12 h 2. TBAF		(73)	126, 127
	 1000%	$Pd(OAc)_2$ (10%), THF, rt, 24 h		(55)	21, 325
C_{13}					
	 120%	1. *t*-BuOCu (120%), DMF, rt, 10 h 2. TBAF		(76)	126, 127

C_{14}

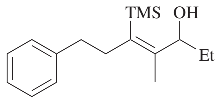
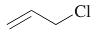
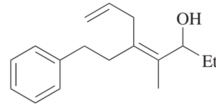
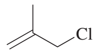
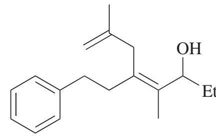
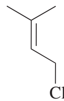
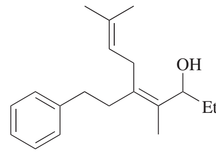
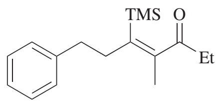
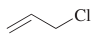
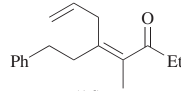
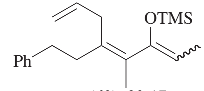
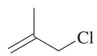
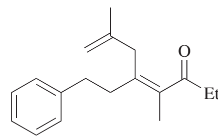
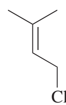
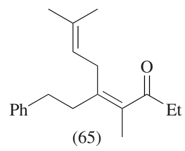
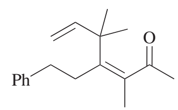
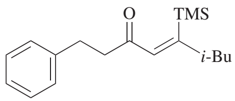
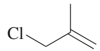
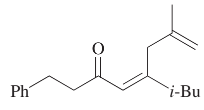
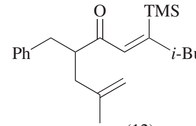
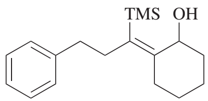
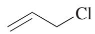
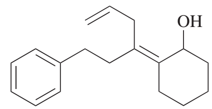
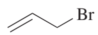
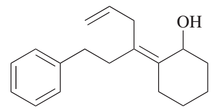
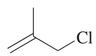
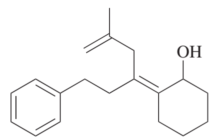
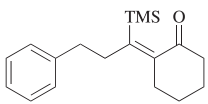
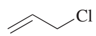
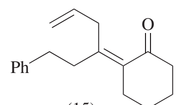
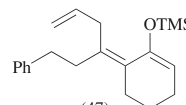
	 120%	1. *t*-BuOCu (150%), THF, rt, 14 h 2. TBAF	 (80)	126, 127
	 120%	1. *t*-BuOCu (150%), THF, rt, 21 h 2. TBAF	 (85)	126, 127
	 120%	1. *t*-BuOCu (120%), DMF, rt, 4 h 2. TBAF	 (75)	126, 127
		CuCl (50%), *t*-BuOLi (120%), DMF/THF, 0° to rt, 2 h	 (16) +  (69), 83:17	130
		CuCl (50%), *t*-BuOLi (120%), DMF/THF, 0° to rt, 2 h	 (76)	130
		CuCl (50%), *t*-heptOLi (120%), DMF/THF, 0° to rt, 2 h	 (65) +  (4)	130

TABLE 3D. CROSS-COUPLING OF ALKENYLSILANES WITH ALLYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
		CuCl (300%), *t*-heptOLi (300%), DMF/THF, 0° to rt, 2 h	 (62) +  (12)	130
	 120%	1. *t*-BuOCu (150%), THF, rt, 16 h 2. TBAF	 (88)	126, 127
	 120%	1. *t*-BuOCu (150%), THF, rt, 16 h 2. TBAF	 (89)	446
	 120%	1. *t*-BuOCu (150%), DMF, rt, 2 h, 2. TBAF	 (84)	126, 127
		CuCl (50%), *t*-heptOLi (120%), DMF/THF, 0° to rt, 1 h	 (15) +  (47)	130

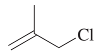
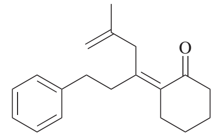
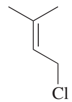
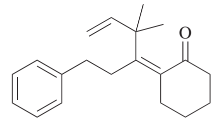
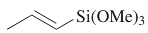
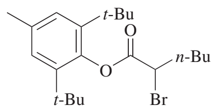
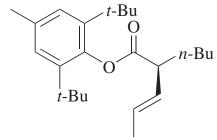
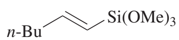
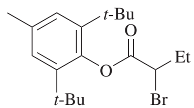
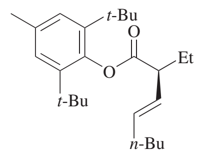
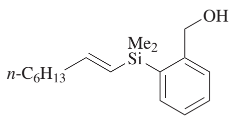
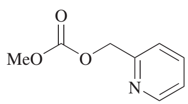
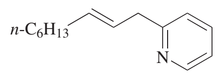
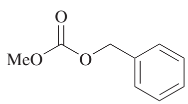
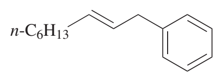
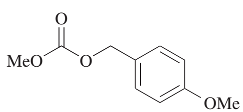
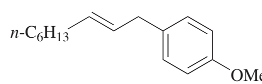
	1. CuCl (50%), *t*-BuOLi (120%), DMF/THF, 0° to rt, 2 h 2. TBAF		(80)	130
	CuCl (50%), *t*-heptOLi (120%), DMF/THF, 0° to rt, 1 h		(63)	130

TABLE 3E. CROSS-COUPLING OF ALKENYLSILANES WITH ALKYL/BENZYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt		(66) 93% ee	118
C_6					
		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt		(70) 91% ee	118
C_8					
		Cp(allyl)Pd (5%), dppf (5%), THF, 80°, 40 h		(75)	152
		Cp(allyl)Pd (5%), dppf (5%), THF, 80°, 18 h		(87)	152
		Cp(allyl)Pd (5%), dppf (5%), THF, 80°, 10 h		(89)	152

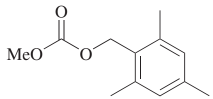
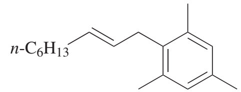
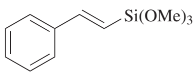
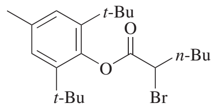
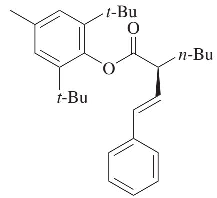
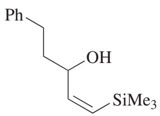
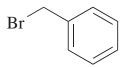
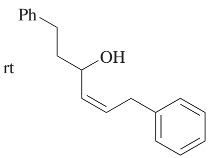
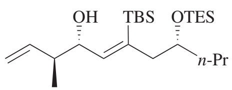
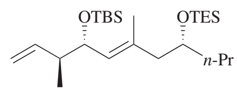
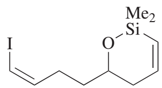
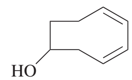
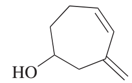
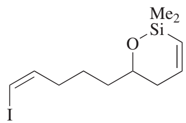
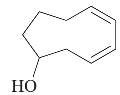
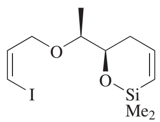
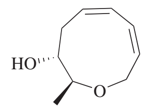
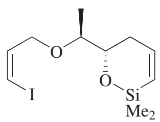
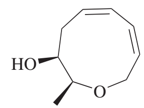
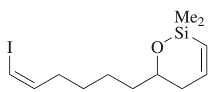
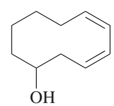
		Cp(allyl)Pd (5%), dppf (5%), THF, 80°, 10 h		(86)	152
C_8					
		$NiCl_2$•glyme (10%), **L3** (12%), TBAT (200%), dioxane, rt		(92) 72% ee	118
C_{11}					
 (*Z*)/(*E*) = 97:3	 120%	1. CuO*t*-Bu (100%), DMF, rt 2. TBAF (100%)		(60)	128
C_{12}					
	MeI	1. *n*-BuLi, –78° 2. MeI, CuBr•Me_2S, DMPU, –78° to rt		(—)	129

TABLE 3F. INTRAMOLECULAR CROSS-COUPLING OF ALKENYLSILANES

Silane	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	$[allylPdCl]_2$ (7.5%), TBAF (1000%), THF, rt, 60 h	 (30) +  (30)	226, 227
C_9			
	$[allylPdCl]_2$ (7.5%), TBAF (1000%), THF, rt, 45 h	 (70)	226, 227
	$[allylPdCl]_2$ (7.5%), TBAF (1000%), THF, rt, 45 h	 (77)	226, 227
	$[allylPdCl]_2$ (7.5%), TBAF (1000%), THF, rt, 45 h	 (72)	226, 227
C_{10}			
	$[allylPdCl]_2$ (7.5%), TBAF (1000%), THF, rt, 45 h	 (63)	226, 227

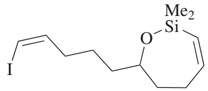
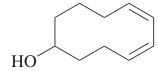
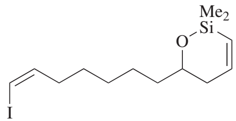
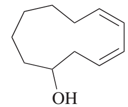
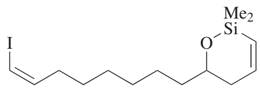
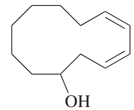
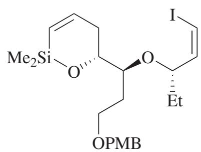
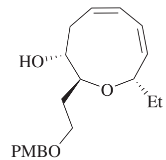
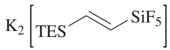
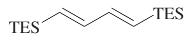
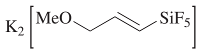
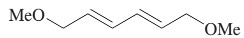
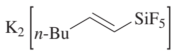
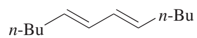
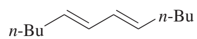
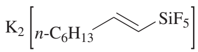
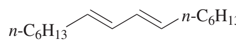
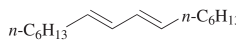
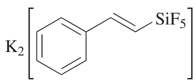
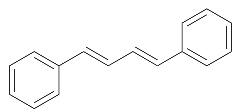
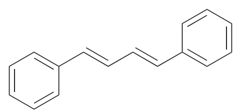
	$[allylPdCl]_2$ (10%), TBAF (1000%), THF, rt, 60 h		(71)	226, 227
C_{11}				
	$[allylPdCl]_2$ (10%), TBAF (1000%), THF, rt, 75 h		(55)	226, 227
C_{12}				
	$[allylPdCl]_2$ (10%), TBAF (1000%), THF, rt, 75 h		(72)	226, 227
	$[allylPdCl]_2$ (7.5%), TBAF, rt, 60 h		(61)	228, 229

TABLE 3G. HOMODIMERIZATION OF ALKENYLSILANES

Silane	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2				
	AgF (100%), MeCN, rt		(58)	273
C_3				
	aq. $AgNO_3$ (110%), Et_2O, rt		(51)	273
C_6				
	AgF (100%), MeCN, rt		(63)	273
	CuCl, 200°, 20 mmHg		(30) 96% (*E*,*E*)	272
C_8				
	AgF (100%), MeCN, rt		(74)	273
	CuCl, 250°, 3 mmHg		(35) 95% (*E*,*E*)	272
	CuCl, 250°, 3 mmHg		(64)	272
	$PdCl_2$, MeCN, 3 h		(54)	21

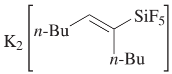
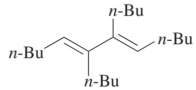
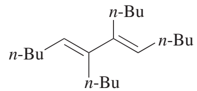
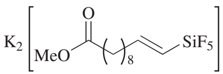
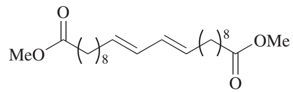
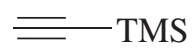
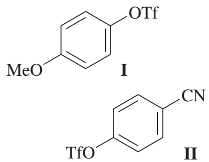
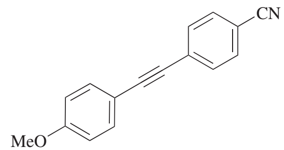
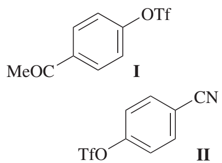
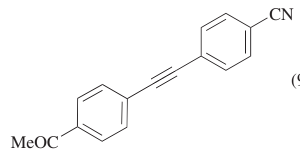
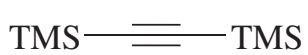
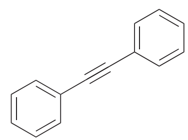
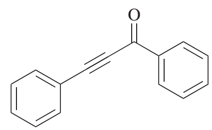
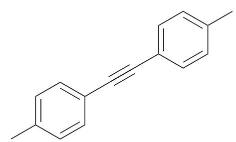
C_{10}				
	AgF (100%), MeCN, rt		(72)	273
	CuCl, 200°, 3 mmHg		(43) (*E*,*E*)/other isomers = 92:8	272
C_{11}				
	aq. $AgNO_3$ (110%), Et_2O, rt		(65)	273

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 I, II	1. **I**, $Pd(PPh_3)_4$ (10%), NEt_3/DMF 60°, 6 h 2. **II**, CuCl (10%), DMF, 80°, 12 h	 (80)	131
	 I, II	1. **I**, $Pd(PPh_3)_4$ (10%), NEt_3/DMF 60°, 6 h 2. **II**, CuCl (10%), DMF, 80°, 12 h	 (94)	131
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h	 (77)	132
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h	 (66)	132
	$(p\text{-tol})_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h	 (80)	132

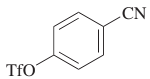
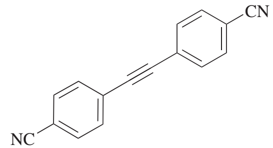
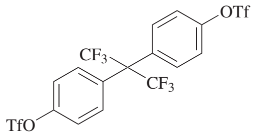
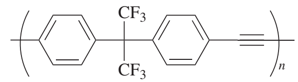
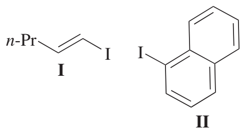
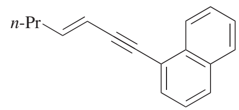
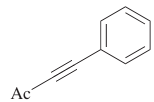
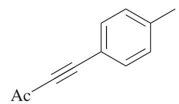
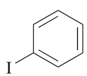
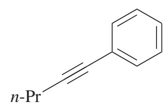
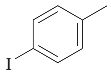
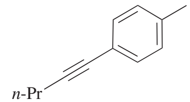
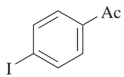
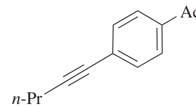
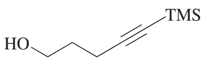
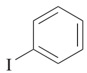
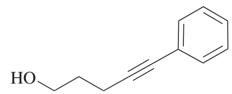
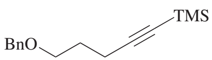
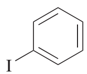
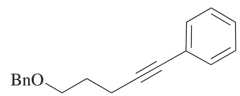
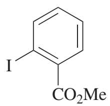
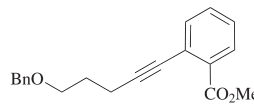
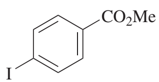
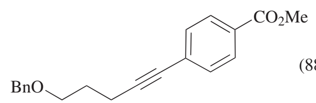
		$Pd(PPh_3)_4$ (10%), CuCl (20%), DMF 80°, 12 h	 (86)	133
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 16 h	 (63) $M_n = 9700$	147
Me_3Sn—≡—TMS		1. **I**, $Pd(PPh_3)_4$ (5%), DMF, 50°, 1.5 h 2. **II**, TASF (200%), DMF, –78 to 50°, 2 h	 (63)	134
C_4				
Ac—≡—TMS	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3•CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h	 (85)	132
	$(p\text{-tol})_3Sb(OAc)_2$	$Pd_2(dba)_3•CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h	 (82)	132
C_5				
n-Pr—≡—$SiMe_2OH$		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h	 (95)	138

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_5					
n-Pr—≡—SiMe$_2$OH		Pd(PPh$_3$)$_4$ (5%), TBAF (100%), THF, 60°, 3 h		(90)	138
		Pd(PPh$_3$)$_4$ (5%), TBAF (100%), THF, 60°, 2 h		(72)	138
		Pd(PPh$_3$)$_4$ (10%), AgCl (20%), MeOH (800%), K$_2$CO$_3$ (800%), DMF, 40°, 19 h		(71)	143
		CuCl (200%), Bu$_3$N (300%), DMI, 120°		(60)	139
		CuCl (200%), Bu$_3$N (300%), DMI, 120°		(84)	139
		CuCl (200%), Bu$_3$N (300%), DMI, 120°		(88)	139

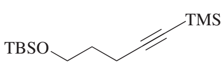
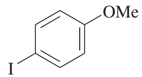
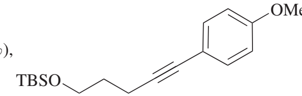
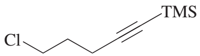
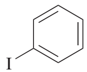
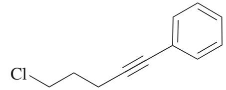
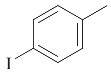
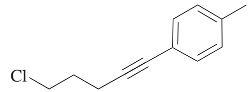
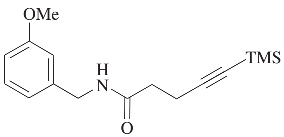
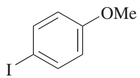
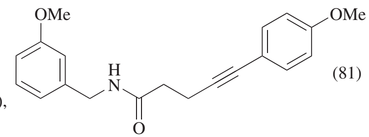
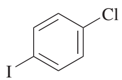
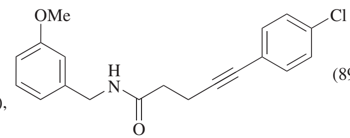
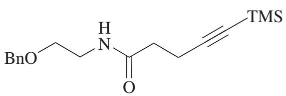
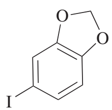
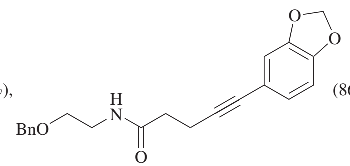
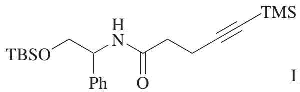
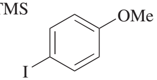
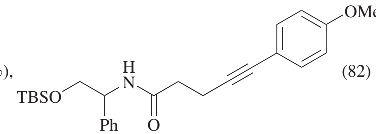
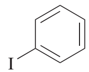
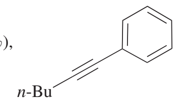
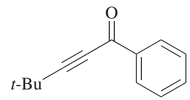
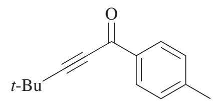
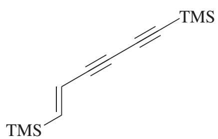
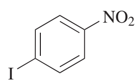
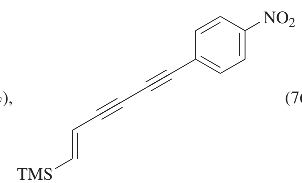
		Ag_2CO_3 (50%), $Pd(OAc)_2$ (5%), PPh_3 (20%), TBAC (100%), THF, 65°, 2 h		(84)	137
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h		(66)	138
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h		(62)	138
		Ag_2CO_3 (50%), $Pd(OAc)_2$ (5%), PPh_3 (20%), TBAC (100%), THF, 65°, 2 h		(81)	137
		Ag_2CO_3 (50%), $Pd(OAc)_2$ (5%), PPh_3 (20%), TBAC (100%), THF, 65°, 2 h		(89)	137
		Ag_2CO_3 (50%), $Pd(OAc)_2$ (5%), PPh_3 (20%), TBAC (100%), THF, 65°, 2 h		(86)	137

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		Ag_2CO_3 (50%), $Pd(OAc)_2$ (5%), PPh_3 (20%), TBAC (100%), THF, 65°, 2 h	 (82)	137
C_6				
n-Bu—≡—TMS		$Pd(PPh_3)_4$ (10%), AgCl (20%), MeOH (400%), K_2CO_3 (400%), DMF, 40°, 20 h	 (99)	143
t-Bu—≡—TMS	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h	 (80)	132
	(*p*-tol)$_3$Sb(OAc)$_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h	 (77)	132
		$Pd(PPh_3)_4$ (5%), AgCl (20%), MeOH (800%), K_2CO_3 (800%), DMF, 40°	 (76)	326

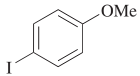
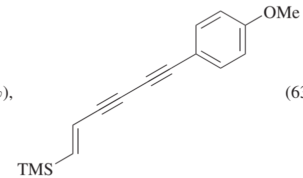
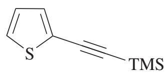
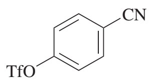
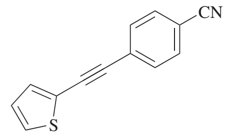
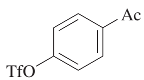
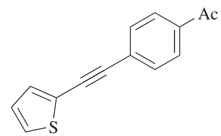
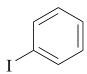
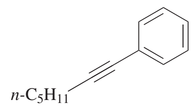
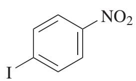
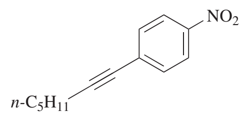
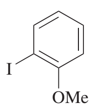
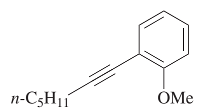
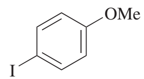
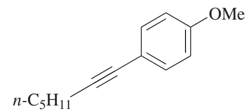
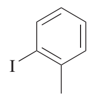
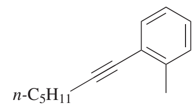
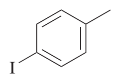
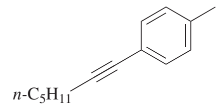
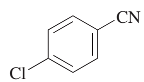
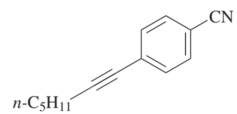
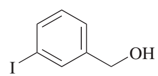
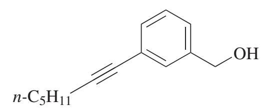
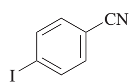
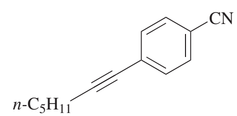
		$Pd(PPh_3)_4$ (5%), AgCl (20%), MeOH (800%), K_2CO_3 (800%), DMF, 40°		(63)	326
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(52)	131, 133
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(43)	133
C_7					
$n\text{-}C_5H_{11}C\equiv CSiMe_2OH$		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(93)	217
		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(83)	217
		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 24 h		(93)	217

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
n-C_5H_{11}—≡—$SiMe_2OH$		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(95)	217
		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 24 h		(93)	217
		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(87)	217
n-C_5H_{11}—≡—TMS		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h		(70)	141
n-C_5H_{11}—≡—$SiMe_2OH$		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(84)	217
		KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h		(75)	217

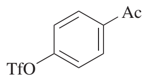
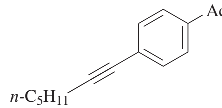
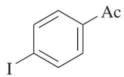
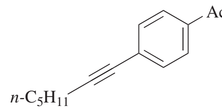
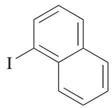
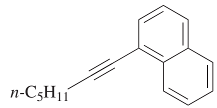
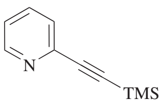
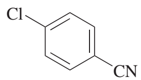
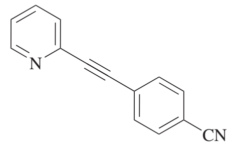
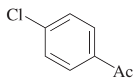
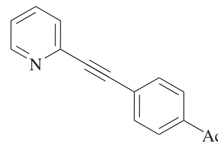
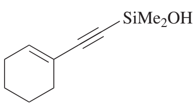
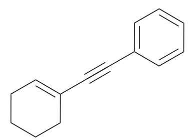
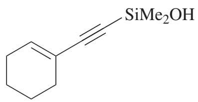
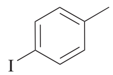
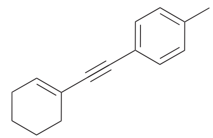
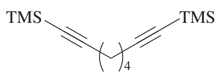
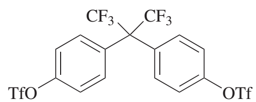
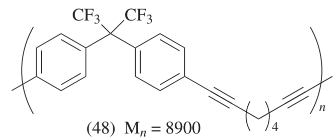
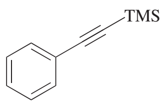
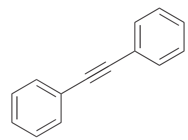
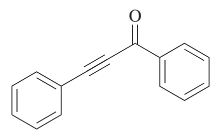
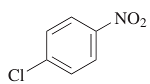
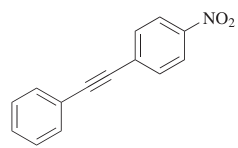
	n-C_5H_{11}—≡—TMS		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°	 (65)	178
			KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h	 (92)	217
			KOTMS (200%), $PdCl_2(PPh_3)_2$ (2.5%), CuI (5%), DME, rt, 3 h	 (93)	217
			$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 48 h	 (38)	141
			$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 48 h	 (37)	141
C_8					
		I—Ph	$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h	 (70)	138

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 1 h		(77)	138
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 37 h	 (48) M_n = 8900		147
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h		(81)	132
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h		(62)	132
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 3 h		(10)	141

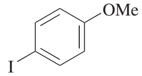
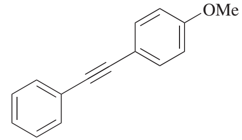
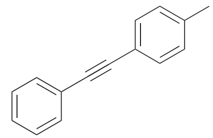
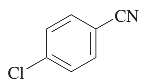
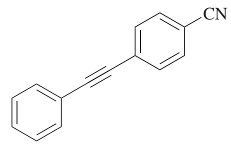
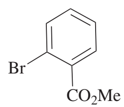
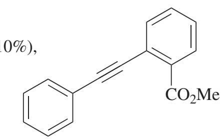
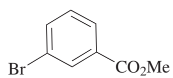
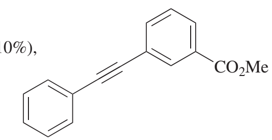
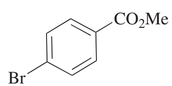
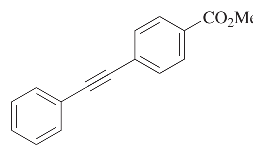
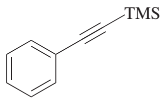
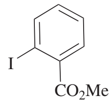
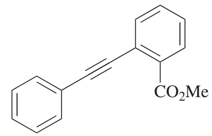
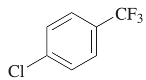
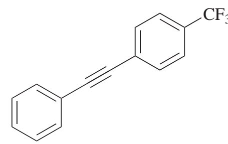
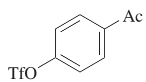
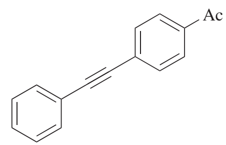
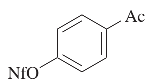
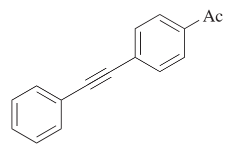
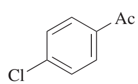
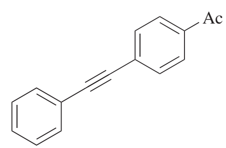
	$Pd(OAc)_2$ (5%), PPh_3 (20%), CuCl (10%), Ag_2CO_3 (50%), TBAC (100%), THF 65°, 2 h		(92)	137
(*p*-tol)$_3$Sb(OAc)$_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h		(80)	132
	$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 6 h		(47)	141
	$Pd(OAc)_2$ (5%), (*o*-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min		(85)	140
	$Pd(OAc)_2$ (5%), (*o*-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min		(84)	140
	$Pd(OAc)_2$ (5%), TBAC (100%), DMF, MW, 100°, 15 min		(7)	140

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$Pd(OAc)_2$ (5%), (o-tol)$_3$P, TBAC (100%), DMF, MW, 100°, 15 min		(85)	140
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 6 h		(34)	141
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF		(89)	131, 133
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(97)	133
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 10 h		(57)	141

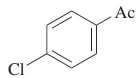
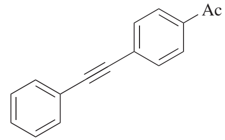
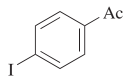
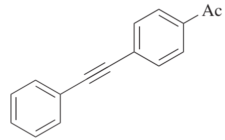
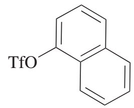
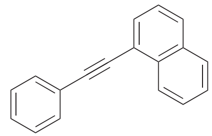
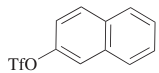
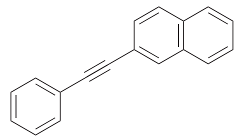
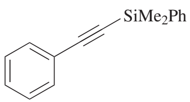
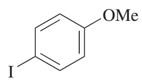
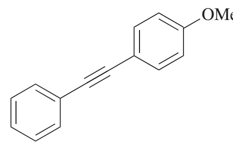
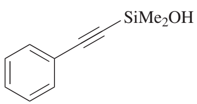
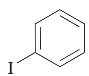
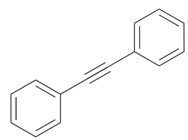
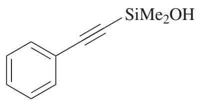
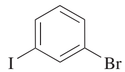
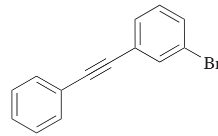
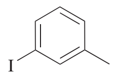
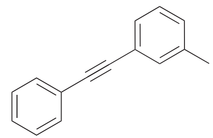
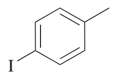
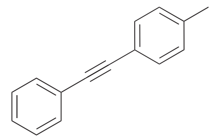
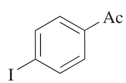
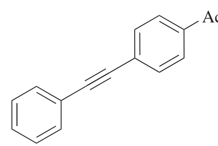
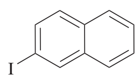
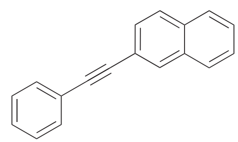
		$PdCl_2$(dppb) (5%), CuCl (10%), DMF, 120°, 12 h		(56)	133
		$[allylPdCl]_2$ (2.5%), TBAF (100%), CO (30 atm), THF, 50°, 20 h		(64)	179
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 14 h		(64)	133
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 12 h		(65)	133
		$[allylPdCl]_2$ (2.5%), TBAF (150%), THF, 60°, 48 h		(30)	162
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2.5 h		(97)	138

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h		(73)	138
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2.5 h		(95)	138
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 3 h		(99)	138
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 2 h		(78)	138
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 3 h		(71)	138

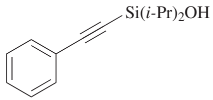
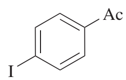
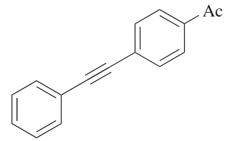
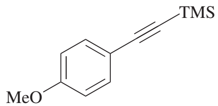
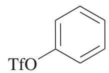
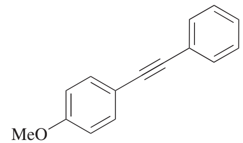
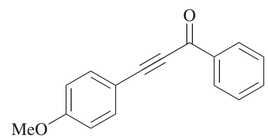
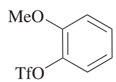
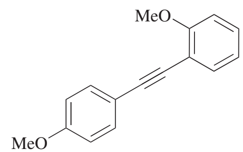
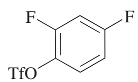
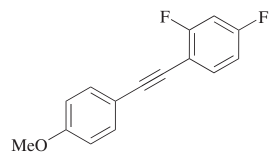
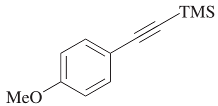
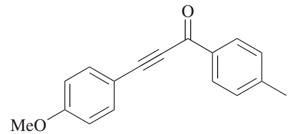
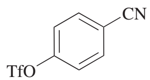
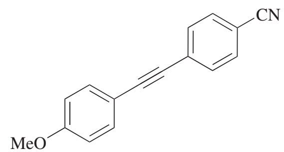
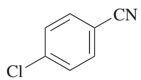
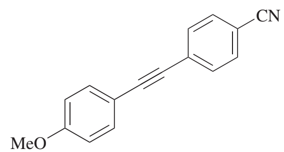
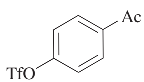
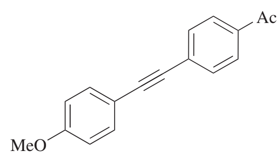
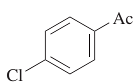
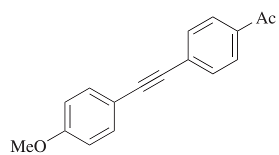
		$Pd(PPh_3)_4$ (5%), TBAF (100%), THF, 60°, 3 h		(52)	138
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(50)	133
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3{\bullet}CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h		(65)	132
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(40)	133
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(79)	133

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
	$(p\text{-tol})_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h		(80)	132
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(51)	131, 133
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h		(71)	141
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(65)	131, 133
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h		(34)	141

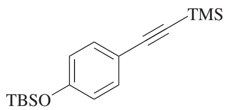
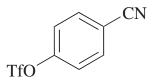
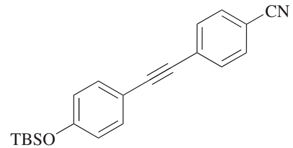
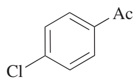
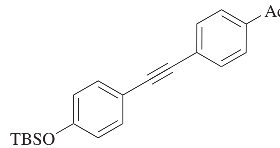
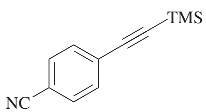
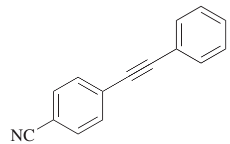
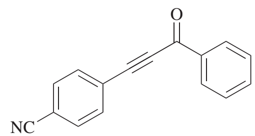
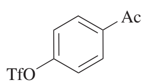
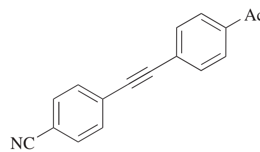
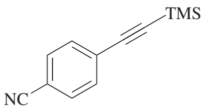
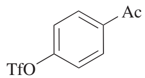
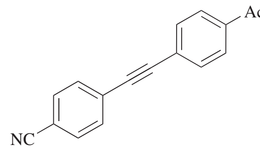
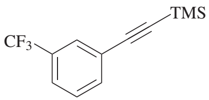
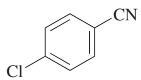
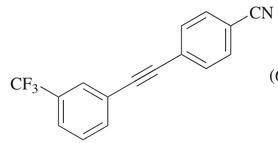
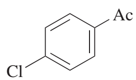
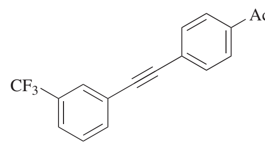
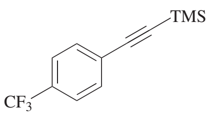
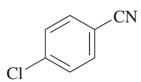
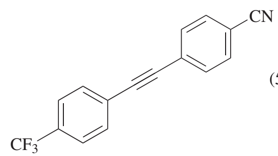
			$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(71)	131, 133
			$Pd(OAc)_2$ (10%), CuCl (10%), (–)-DIOP (10 %), DMF, 120°, 12 h		(50)	141
C_9		$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h		(70)	132
		$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h		(68)	132
			$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°		(52)	131

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°	 (65)	133
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 24 h	 (63)	141
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h	 (48)	141
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 24 h	 (54)	141

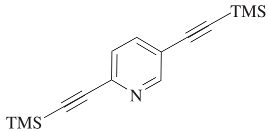
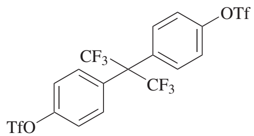
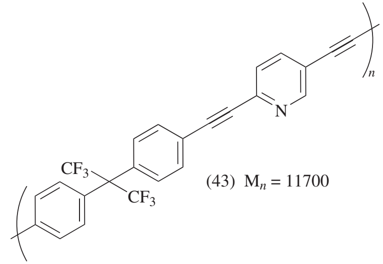
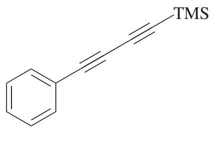
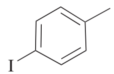
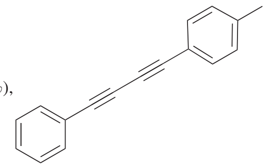
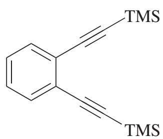
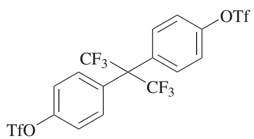
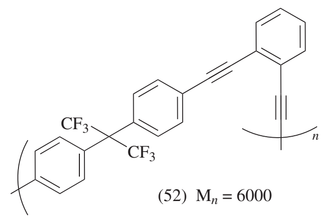
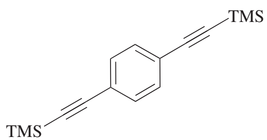
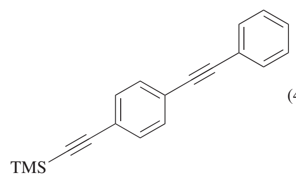
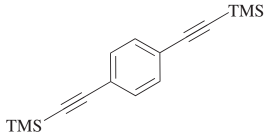
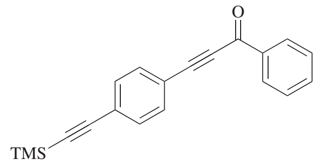
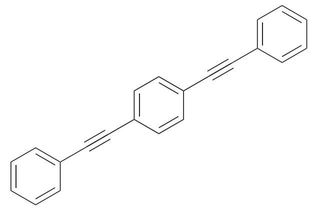
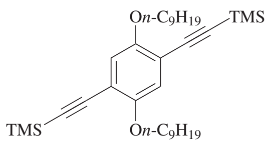
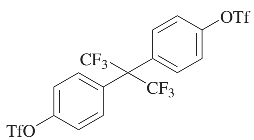
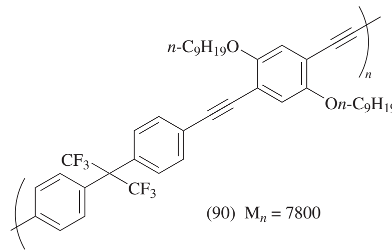
			$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 6 h	 (43) M_n = 11700	147
C_{10}					
			$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°	 (82)	326
			$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 120°, 72 h	 (52) M_n = 6000	147
		$Ph_3Sb(OAc)_2$	$PdCl_2$ (5%), CuI (10%), MeCN, 50°, 5 h	 (42)	132

TABLE 4A. CROSS-COUPLING OF ALKYNYLSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), CO (1 atm), MeCN, 50°, 5 h	 (58)	132
	$Ph_3Sb(OAc)_2$	$Pd_2(dba)_3$•$CHCl_3$ (5%), CuI (10%), MeCN, 50°, 5 h	 (75)	132
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 5 h	 (90) M_n = 7800	147

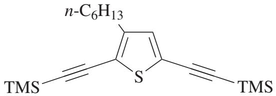
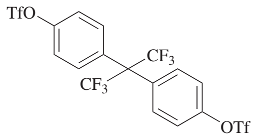
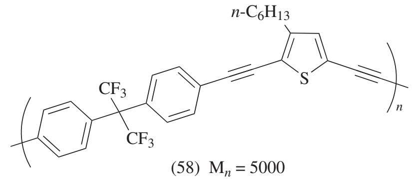
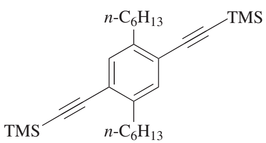
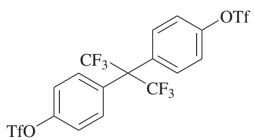
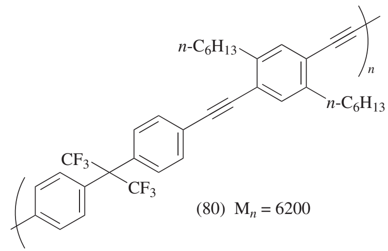
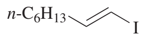
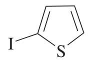
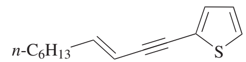
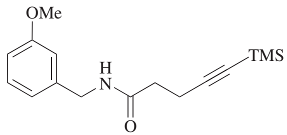
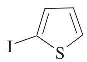
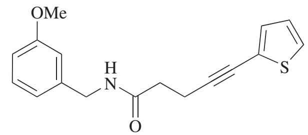
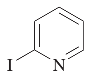
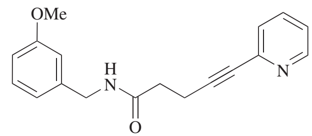
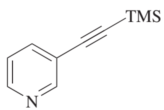
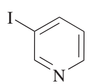
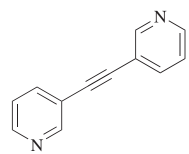
C_{14}				
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 80°, 1 h	 (58) $M_n = 5000$	147
C_{22}				
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 120°, 2 h	 (80) $M_n = 6200$	147

TABLE 4B. CROSS-COUPLING OF ALKYNYLSILANES WITH HETEROARYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
Me_3Sn—≡—TMS	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), DMF 50°, 6 h 2. **II**, TASF (240%), –78 to 50°, 2 h		(55)	134
C_5					
		$Pd(OAc)_2$ (5%), PPh_3 (20%), Ag_2CO_3 (50%), TBAC (100%), 65°, 2 h		(89)	137
		$PdCl_2(PPh_3)_2$ (5%), Ag_2CO_3 (50%), TBAC (100%), 65°, 2 h		(72)	137
C_7					
		$Pd(OAc)_2$ (5%), $(o\text{-tol})_3P$ (10%), TBAC (100%), DMF, MW, 100°, 15 min		(82)	140

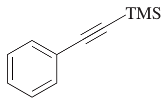
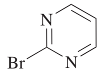
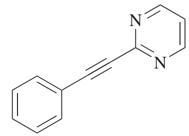
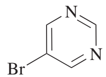
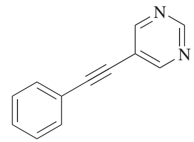
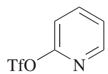
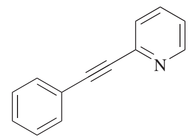
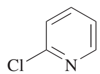
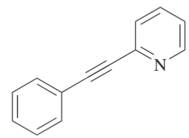
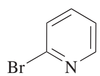
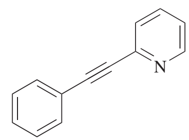
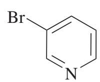
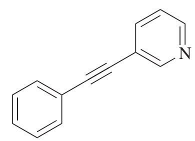
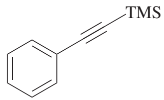
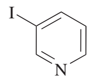
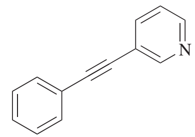
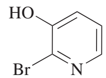
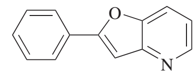
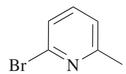
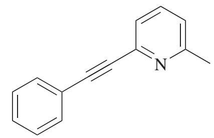
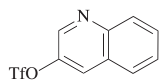
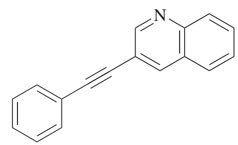
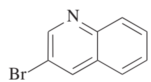
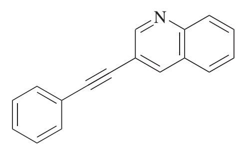
C_8 		$Pd(OAc)_2$ (5%), (o-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min	 (44)	140
		$Pd(OAc)_2$ (5%), (o-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min	 (84)	140
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 40°, 16 h	 (68)	133
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h	 (60)	141
		$Pd(OAc)_2$ (5%), TBAC (100%), DMF, MW, 100°, 15 min	 (39)	140
		$Pd(OAc)_2$ (5%), (o-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min	 (71)	140

TABLE 4B. CROSS-COUPLING OF ALKYNYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
		$Pd(OAc)_2$ (5%), $(o\text{-tol})_3P$ (10%), TBAC (100%), DMF, MW, 100°, 15 min		(90)	140
		$Pd(OAc)_2$ (5%), TBAC (100%), DMF, MW, 100°, 15 min		(33)	140
		$Pd(OAc)_2$ (5%), $(o\text{-tol})_3P$ (10%), TBAC (100%), DMF, MW, 120°, 2.5 min		(50)	140
		$Pd(PPh_3)_4$ (5%), CuCl (10%), DMF, 40°, 9 h		(62)	133
		$Pd(OAc)_2$ (5%), $(o\text{-tol})_3P$ (10%), TBAC (100%), DMF, MW, 100°, 15 min		(57)	140

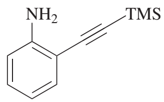
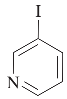
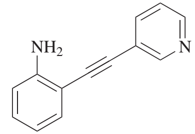
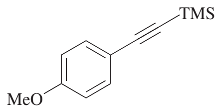
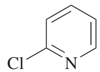
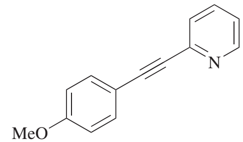
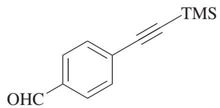
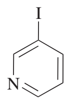
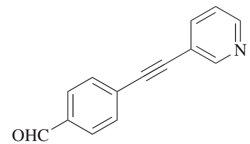
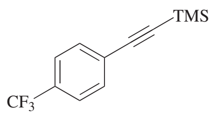
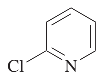
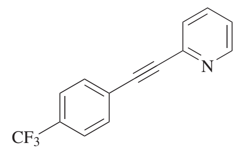
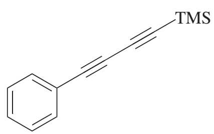
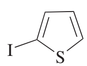
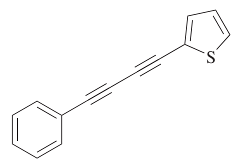
		$Pd(OAc)_2$ (5%), (o-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min		(81)	140
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 3 h		(45)	141
C_9					
		$Pd(OAc)_2$ (5%), (o-tol)$_3$P (10%), TBAC (100%), DMF, MW, 100°, 15 min		(60)	140
		$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 12 h		(65)	141
C_{10}					
		$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°		(87)	326

TABLE 4B. CROSS-COUPLING OF ALKYNYLSILANES WITH HETEROARYL ELECTROPHILES (*Continued*)

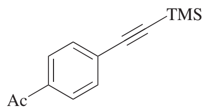
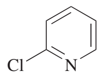
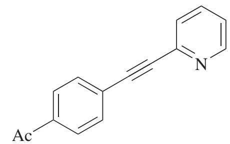
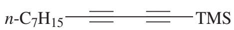
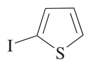
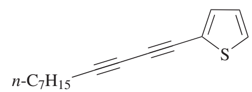
	Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{10}						
			$Pd(OAc)_2$ (10%), (–)-DIOP (10%), CuCl (10%), DMF, 120°, 3 h		(36)	141
C_{11}						
			$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°		(76)	326

TABLE 4C. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKENYL ELECTROPHILES

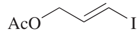
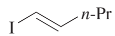
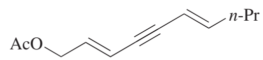
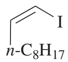
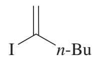
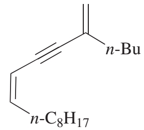
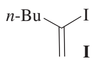
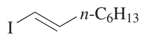
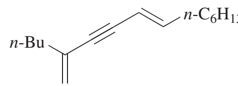
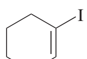
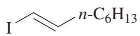
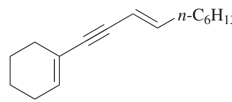
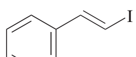
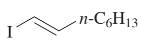
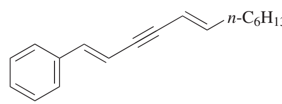
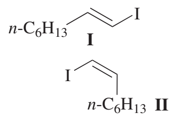
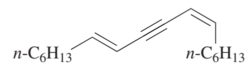
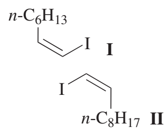
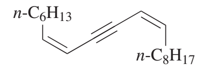
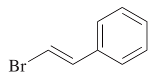
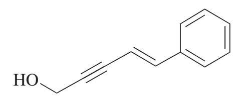
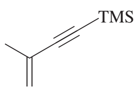
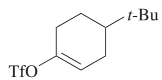
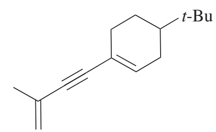
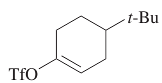
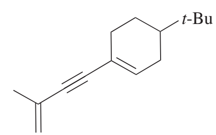
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
$Me_3Sn-C\equiv C-TMS$	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (58)	134
	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (85)	134
	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (80)	134
	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (72)	134
	 **I**  **II**	1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (47)	134

TABLE 4C. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
Me_3Sn—≡—TMS		1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (68)	134
		1. **I**, $Pd(PPh_3)_4$ (5%), THF, 50° 2. **II**, TASF (240%), –78 to 50°	 (70)	134
C_3				
		$[allylPdCl]_2$ (2.5%), TASF (100%), THF	 (84)	23
C_5				
		$Pd(PPh_3)_4$ (10%), AgI (20%), TBAF•$3H_2O$ (150%), 18 h	 (99)	142
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 15 h	 (89)	143

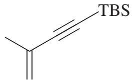
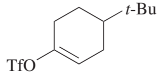
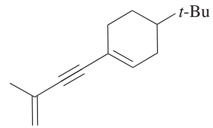
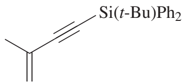
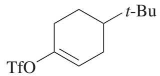
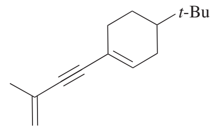
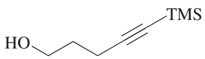
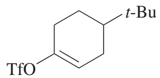
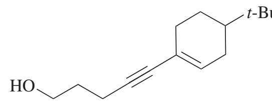
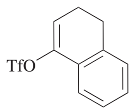
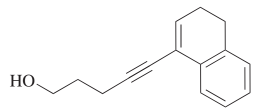
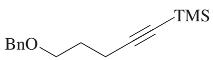
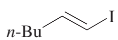
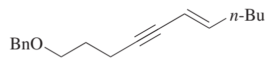
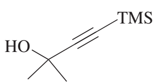
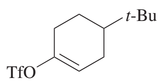
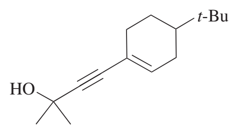
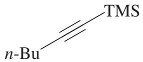
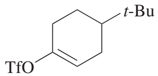
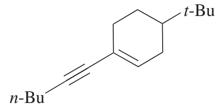
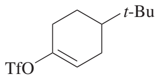
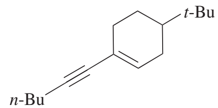
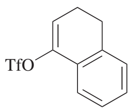
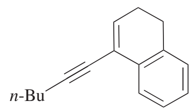
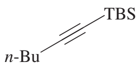
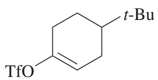
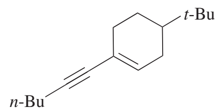
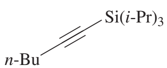
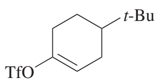
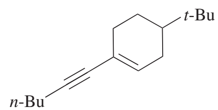
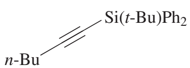
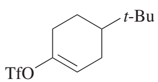
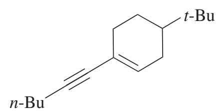
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF{\bullet}3H_2O$ (150%), 18 h		(99)	142
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF{\bullet}3H_2O$ (150%), 18 h		(99)	142
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 19 h		(99)	143
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF		(93)	143
		CuCl (220%), n-Bu_3N (300%), DMI, 100°, 20 h		(88)	139
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 23 h		(78)	143

TABLE 4C. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF•3H_2O$ (150%), 21 h		(87)	142
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 20 h		(99)	143
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF		(96)	143
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF•3H_2O$ (150%), 24 h		(84)	142
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF•3H_2O$ (150%), 24 h		(75)	142
		$Pd(PPh_3)_4$ (10%), AgI (20%), $TBAF•3H_2O$ (150%), 24 h		(75)	142

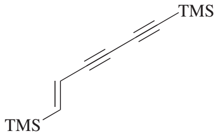
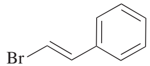
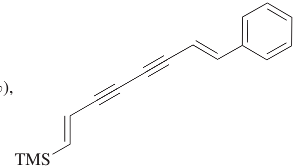
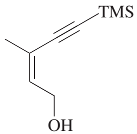
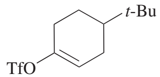
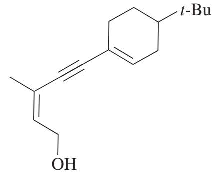
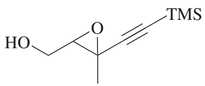
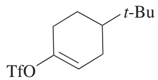
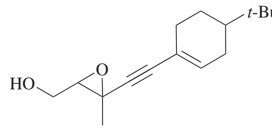
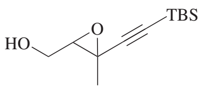
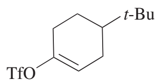
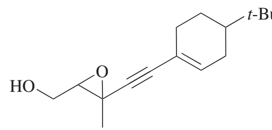
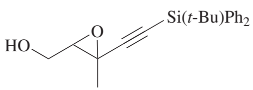
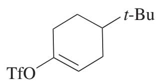
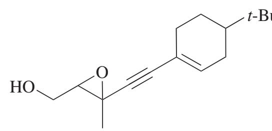
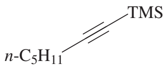
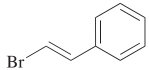
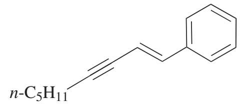
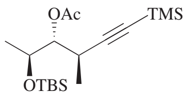
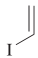
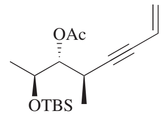
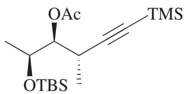
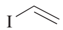
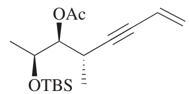
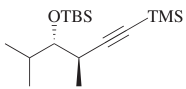
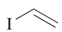
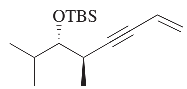
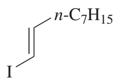
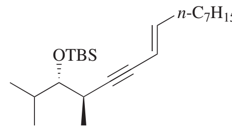
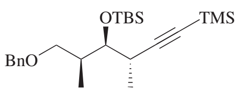
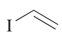
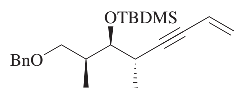
		$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°		(88)	326
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 25 h		(76)	143
		$Pd(PPh_3)_4$ (10%), AgI (20%), TBAF•$3H_2O$ (150%), 22 h		(78)	142
		$Pd(PPh_3)_4$ (10%), AgI (20%), TBAF•$3H_2O$ (150%), 22 h		(67)	142
		$Pd(PPh_3)_4$ (10%), AgI (20%), TBAF•$3H_2O$ (150%), 22 h		(66)	142

TABLE 4C. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_7					
		$[allylPdCl]_2$ (2.5%), TASF (100%), THF		(86)	23
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 3.5 h		(70)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 3.5 h		(64)	139
C_8					
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 19 h		(94)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 5 h		(73)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°		(91)	139

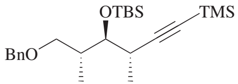
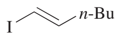
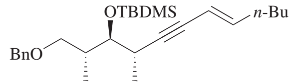
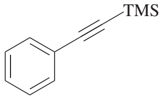
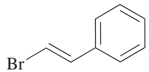
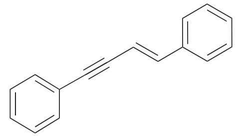
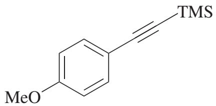
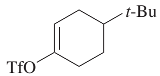
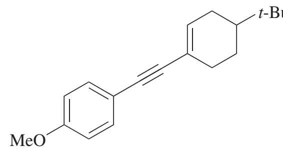
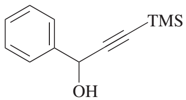
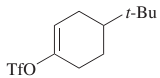
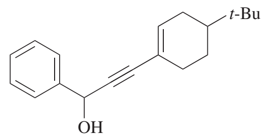
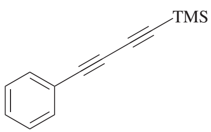
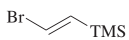
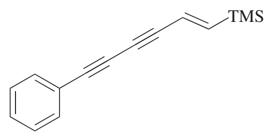
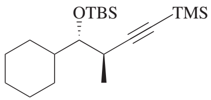
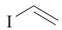
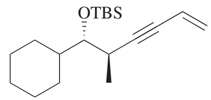
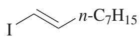
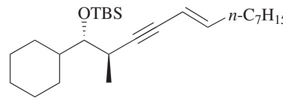
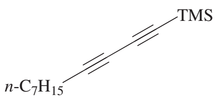
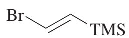
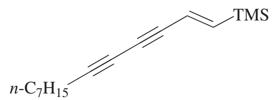
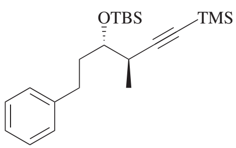
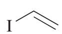
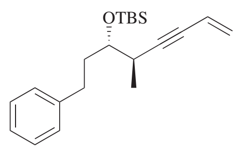
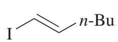
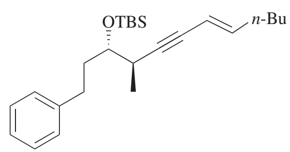
		CuCl (200%), *n*-Bu_3N (300%), DMI, 120°		(90)	139
		$[allylPdCl]_2$ (2.5%), TASF (100%), THF		(83)	23
		CuCl (10%), $Pd(PPh_3)_4$ (5%), DMF, 80°		(90)	131
C_9					
		$Pd(PPh_3)_4$ (10%), AgCl (20%), K_2CO_3 (400%), MeOH (400%), DMF, 22 h		(56)	143
C_{10}					
		$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°		(83)	326

TABLE 4C. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKENYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{11}					
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 14 h		(87)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 3 h		(90)	139
		$Pd(PPh_3)_4$ (5%), AgCl (20%), K_2CO_3 (800%), MeOH (800%), DMF, 40°		(75)	326
C_{13}					
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 16 h		(80)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 3.5 h		(91)	139

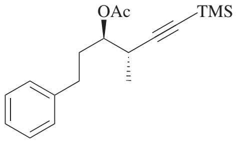
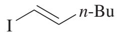
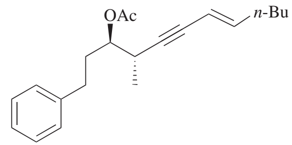
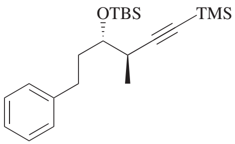
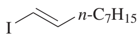
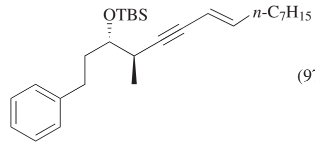
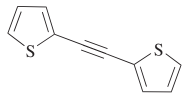
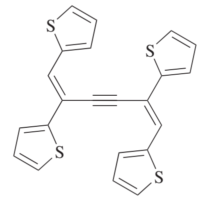
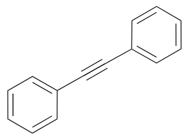
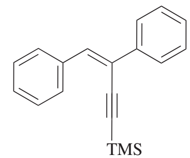
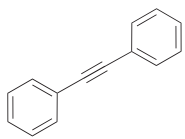
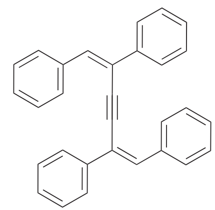
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 3.5 h		(70)	139
		CuCl (200%), n-Bu_3N (300%), DMI, 120°, 4 h		(97)	139

TABLE 4D. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKYNYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
TMS—≡—TMS		1. $[Rh(OH)(cod)]_2$ (5%), dCypb (5 %), 3,4,5-$(MeO)_3C_6H_2OH$ (300%), *o*-xylene, reflux, 2 h 2. KF (20%), 2 h		(60)	327
		$[Rh(OH)(cod)]_2$ (3%), dCypb (3%), PhOH (300%), *o*-xylene, 130°, 6 h		(64)	327
		$[Rh(OH)(cod)]_2$ (5%), dCypb (5%), 3,4,5-$(MeO)_3C_6H_2OH$ (300%), KF (20%), *o*-xylene, reflux, 6 h		(69)	327

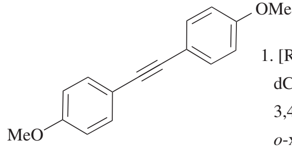
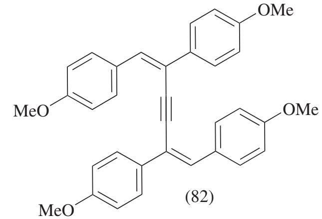
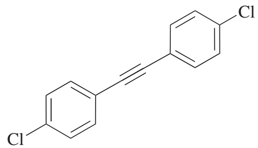
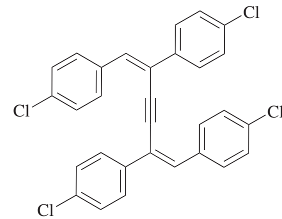
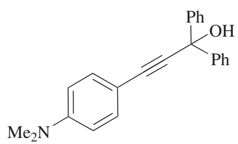
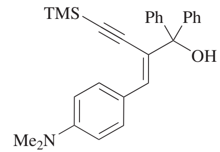
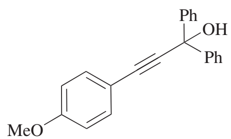
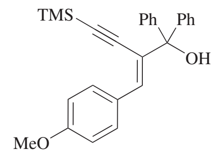
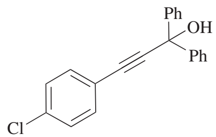
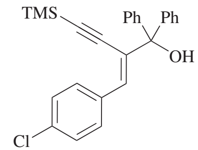
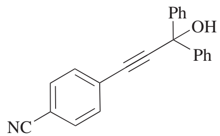
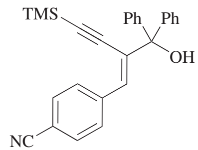
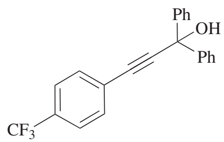
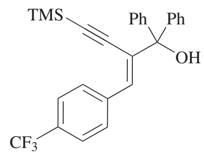
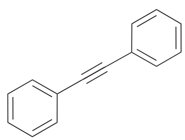
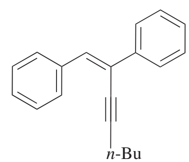
	1. $[Rh(OH)(cod)]_2$ (5%), dCypb (5%), 3,4,5-$(MeO)_3C_6H_2OH$ (300%), *o*-xylene, reflux, 2 h 2. KF (20%), 2 h		(82)	327
	$[Rh(OH)(cod)]_2$ (3%), dCypb (3%), PhOH (300%), *o*-xylene, 130°, 6 h		(22)	327
	$[Rh(OH)(cod)]_2$ (4%), dppb (4%), toluene, 4 h		(82)	328
	$[Rh(OH)(cod)]_2$ (4%), dppb (4%), toluene, 4 h		(83)	328

TABLE 4D. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKYNYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_2					
TMS—≡—TMS		$[Rh(OH)(cod)]_2$ (4%), dppb (4%), toluene, 4 h		(87)	328
		$[Rh(OH)(cod)]_2$ (4%), dppb (4%), toluene, 4 h		(57)	328
		$[Rh(OH)(cod)]_2$ (4%), dppb (4%), toluene, 4 h		(73)	328
C_6					
n-Bu—≡—TMS		$[Rh(OH)(cod)]_2$ (3%), dCypb (3%), 3,4,5-$(MeO)_3C_6H_2OH$ (200%), *o*-xylene, reflux, 12 h		(30)	327

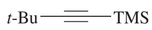
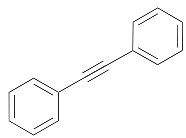
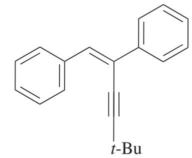
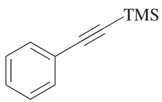
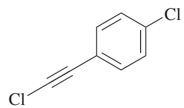
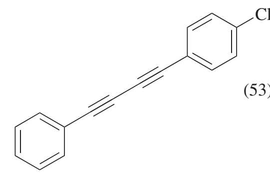
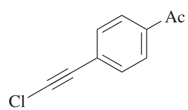
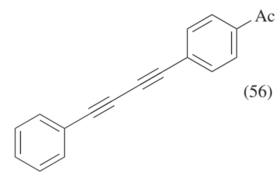
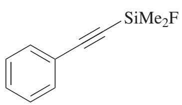
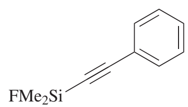
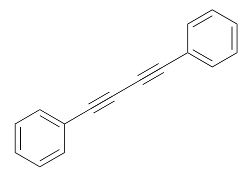
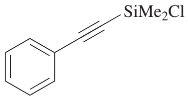
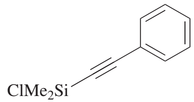
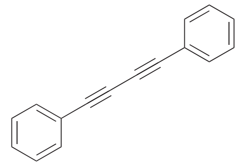
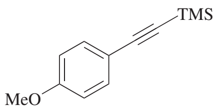
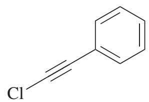
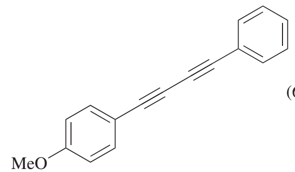
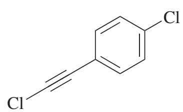
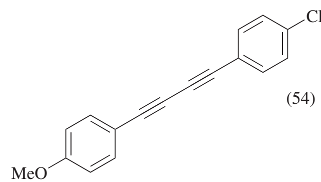
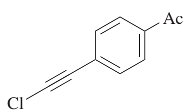
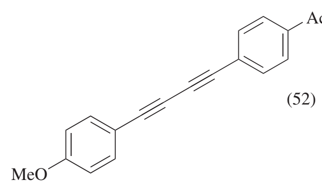
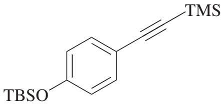
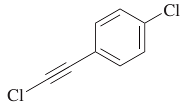
			[Rh(OH)(cod)]$_2$ (3%), dCypb (3%), 3,4,5-(MeO)$_3$C$_6$H$_2$OH (200%), *o*-xylene, reflux, 12 h	 (89)	327
C_8					
			CuCl (10%), DMF, 80°, 48 h	 (53)	133, 144
			CuCl (10%), DMF, 80°, 48 h	 (56)	133, 144
			CuCl (5%), TBAF (118%), MeCN, rt, 5 min	 (94)	178

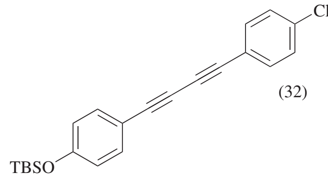
TABLE 4D. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKYNYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		CuCl (5%), TBAF (118%), MeCN, rt, 5 min	 (91)	178
		CuCl (5%), DMF, 80°, 48 h	 (65)	133, 144
		CuCl (5%), DMF, 80°, 48 h	 (54)	133, 144
		CuCl (5%), DMF, 80°, 48 h	 (52)	133, 144



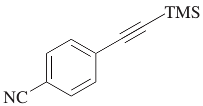


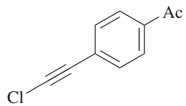
CuCl (5%), DMF, 80°, 48 h



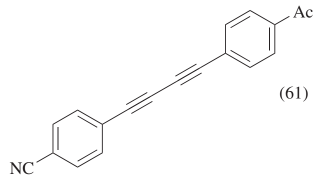
(32) 133, 144

C_9





CuCl (5%), DMF, 80°, 48 h



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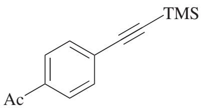
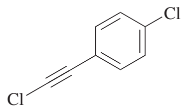
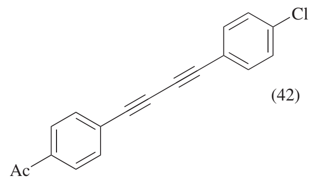
C_{10}

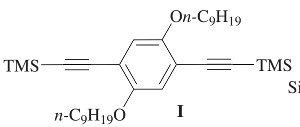




CuCl (5%), DMF, 80°, 48 h



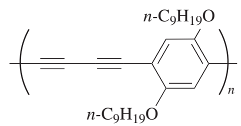
(42) 133, 144



I

Silane **I**

CuCl (100 %), DMF, 80°, 3 h



(77) 329

$M_n = 5100$

TABLE 4D. CROSS-COUPLING OF ALKYNYLSILANES WITH ALKYNYL ELECTROPHILES (*Continued*)

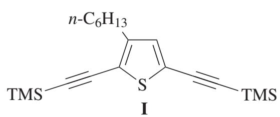
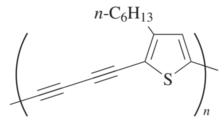
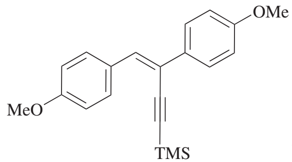
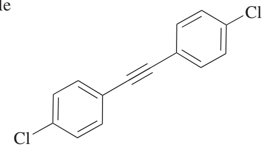
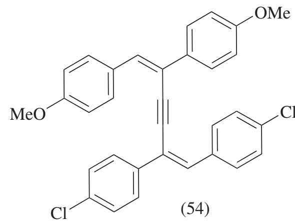
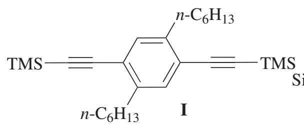
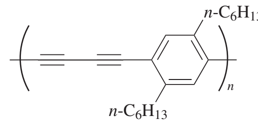
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
	Silane **I**	CuCl (100%), DMF, 60°, 4 h	 (94) M_n = 4000	329
C_{16}				
		$[Rh(OH)(cod)]_2$ (5%), dCypb (5%), 3,4,5-$(MeO)_3C_6H_2OH$ (300%), KF (20%), *o*-xylene, 130°, 12 h	 (54)	327
C_{22}				
	Silane **I**	CuCl (100 %), DMF, 80°, 36 h	 (45) M_n = 7900	329

TABLE 4E. CROSS-COUPLING OF ALKYNYLSILANES WITH ALLYL/PROPARGYL ELECTROPHILES

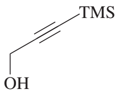
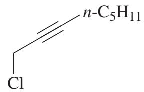
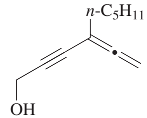
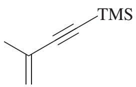
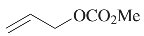
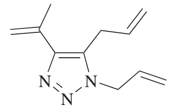
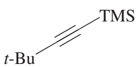
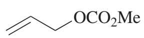
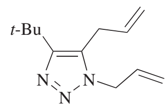
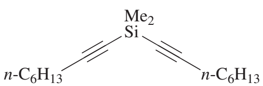
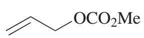
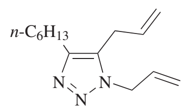
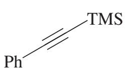
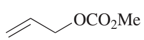
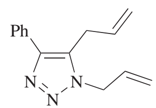
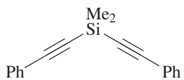
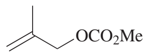
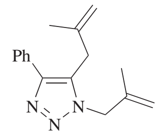
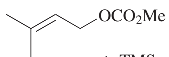
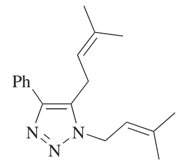
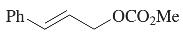
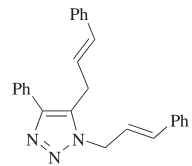
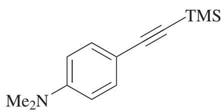
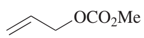
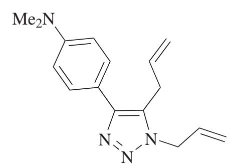
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (64)	145
C_5				
	 + TMS−N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 5 h	 (69)	146
C_6				
	 + TMS−N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 24 h	 (51)	146
C_8				
	 + TMS−N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 4 h	 (63)	146
	 + TMS−N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 8 h	 (77)	146

TABLE 4E. CROSS-COUPLING OF ALKYNYLSILANES WITH ALLYL/PROPARGYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 150°, 2 h		(51)	146
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 150°, 2 h		(34)	146
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 120°, 2 h		(70)	146
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 5 h		(75)	146

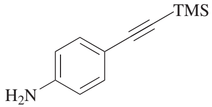
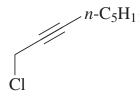
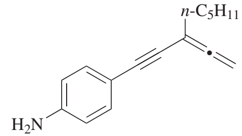
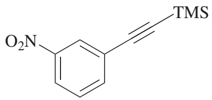
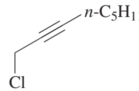
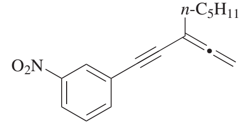
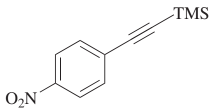
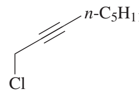
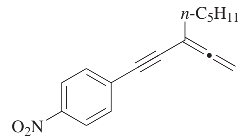
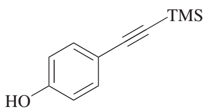
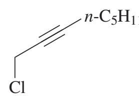
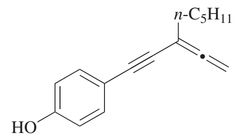
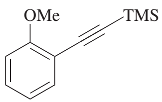
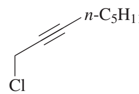
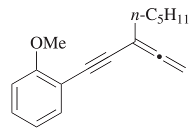
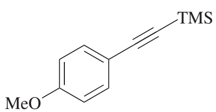
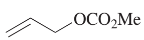
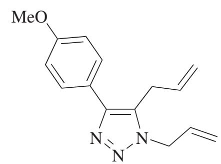
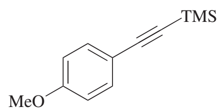
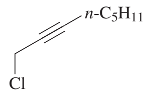
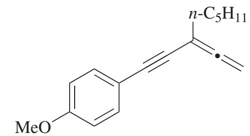
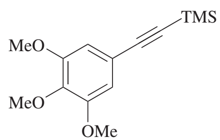
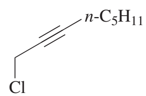
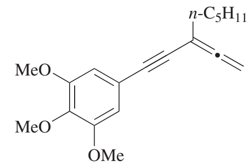
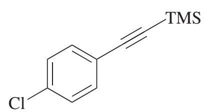
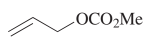
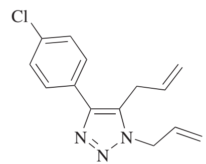
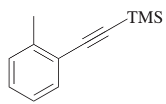
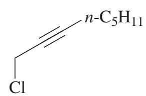
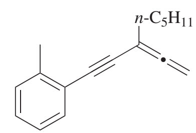
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h		(53)	145
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h		(60)	145
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h		(60)	145
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h		(51)	145
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h		(64)	145
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 5 h		(67)	146

TABLE 4E. CROSS-COUPLING OF ALKYNYLSILANES WITH ALLYL/PROPARGYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (66)	145
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (63)	145
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 10 h	 (71)	146
C_9				
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (67)	145

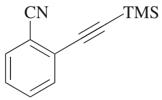
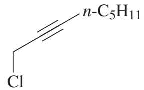
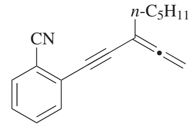
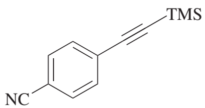
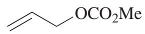
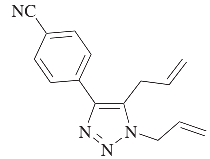
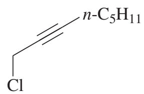
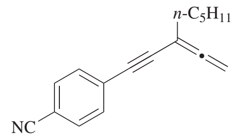
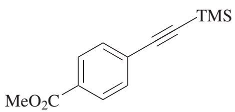
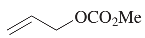
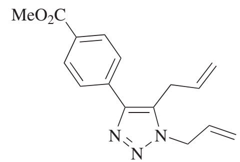
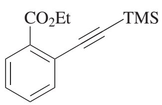
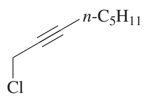
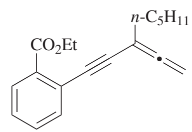
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (57)	145
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 15 h	 (57)	146
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (53)	145
	 + TMS—N_3	$Pd_2(dba)_3$•$CHCl_3$ (2.5%), $P(OEt)_3$ (20%), CuCl (10%), dioxane, 100°, 13 h	 (66)	146
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (61)	145

TABLE 4E. CROSS-COUPLING OF ALKYNYLSILANES WITH ALLYL/PROPARGYL ELECTROPHILES (*Continued*)

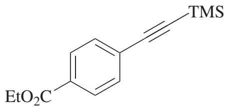
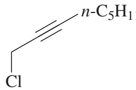
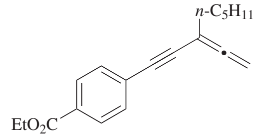
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
		$PdCl_2(PPh_3)_2$ (5%), CuI (100%), TBAF (100%), DMF, 1 h	 (59)	145

TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES

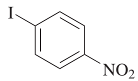
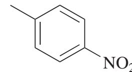
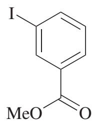
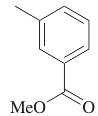
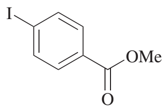
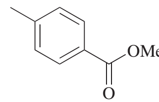
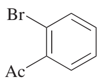
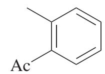
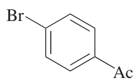
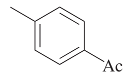
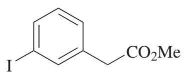
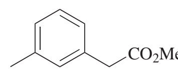
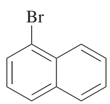
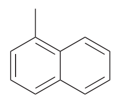
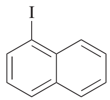
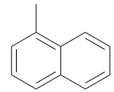
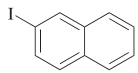
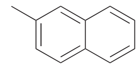
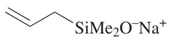
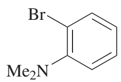
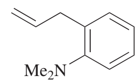
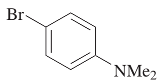
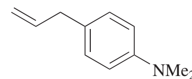
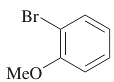
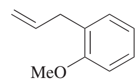
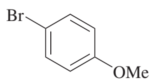
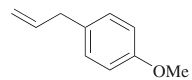
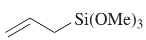
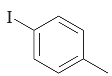
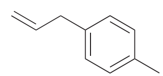
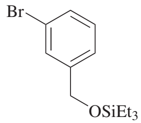
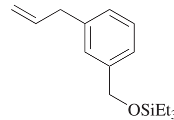
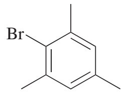
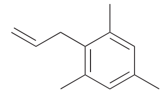
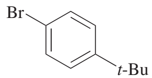
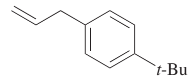
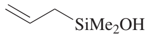
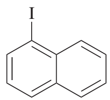
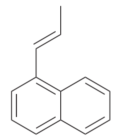
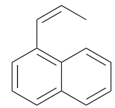
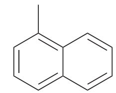
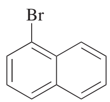
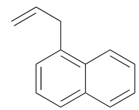
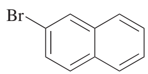
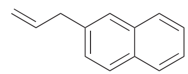
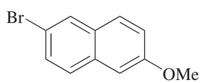
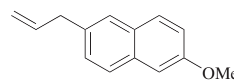
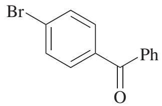
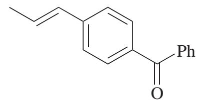
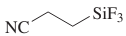
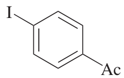
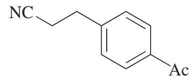
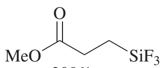
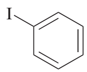
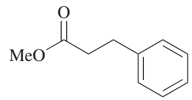
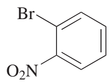
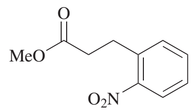
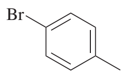
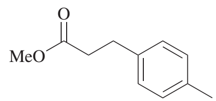
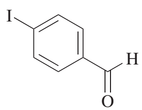
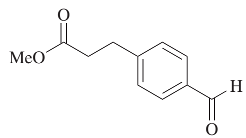
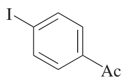
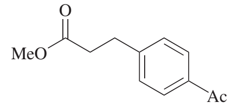
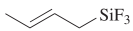
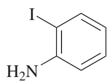
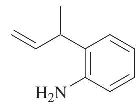
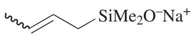
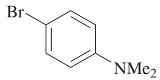
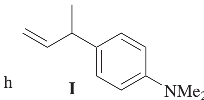
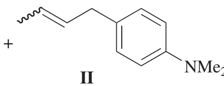
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1				
$(Et_2N)_3S^+ Me_3SiF_2^-$ 200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (86)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (67)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (84)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (17)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (82)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (59)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h	 (13)	275

TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES (*Continued*)

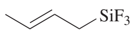
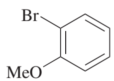
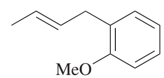
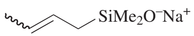
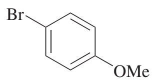
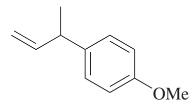
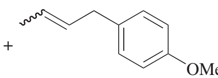
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_1					
$(Et_2N)_3S^+ Me_3SiF_2^-$ 200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h		(78)	275
200%		$[allylPdCl]_2$ (2.5%), THF, 50°, 20 h		(81)	275
C_3					
 250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 12 h		(73)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 7 h		(84)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 12 h		(78)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 3 h		(80)	108
 222%		$Pd(dba)_2$ (9%), TBAF (231%), DMF, 85°		(60)	70

 250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 4 h	 (86)	108
500%		$[allylPdCl_2]_2$ (2.5%), dioxane, 100°, 7 h	 (80)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 9 h	 (74)	108
		$[allylPdCl]_2$ (2.5%), $Cy_3P(O)$ (10%), *t*-BuOK (200%), THF, 60°	 **I** +  **II** +  **III** **I** + **II** + **III** (22), **I**:**II**:**III** = 5.8:1:1.6	108
 250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 2 h	 (85)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 9 h	 (71)	108
250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 6 h	 (95)	108

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_3					
 250%		$[allylPdCl_2]_2$ (2.5%), DME, 85°, 1 h		(76)	108
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 21 h		(87)	190
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 48 h		(75)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 10 h		(32)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 48 h		(62)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 11 h		(76)	190

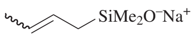
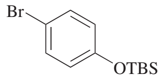
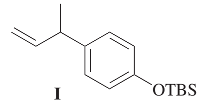
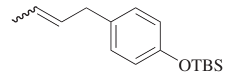
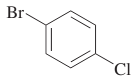
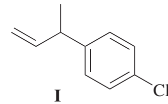
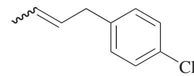
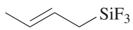
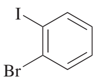
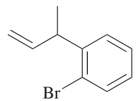
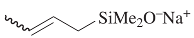
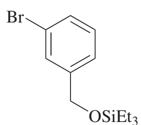
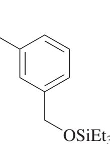
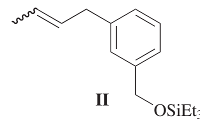
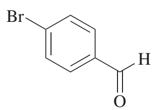
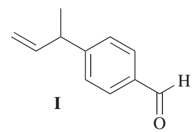
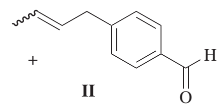
200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 8 h	 (77)	190
C_4				
 150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 100°	 (53)	109
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 6 h	 **I** +  **II**	108

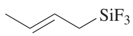
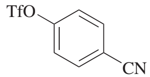
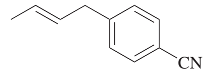
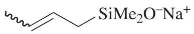
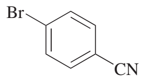
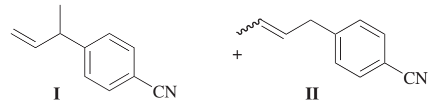
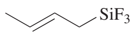
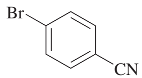
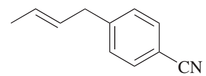
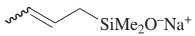
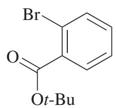
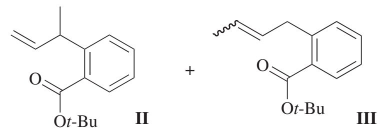
Temp (°)	**I + II**	**I:II**
85	(33)	8.5:1
110	(46)	7.0:1

 400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 12 h	 (58) $(E)/(Z)$ = 6.5:1	110
 200% **I**		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 110°, 3 h	 **II** +  **III**	108

I $(E)/(Z)$	**II + III**	**II:III**
80:20	(46)	7.2:1
>97:3	(46)	18:1
<4:96	(59)	4.0:1

TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 8 h	 **I** +  **II** **I** + **II** (76), **I**:**II** = 13:1	108
200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 5 h	 **I** +  **II** **I** + **II** (67), **I**:**II** = 12:1	108
 150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 100°	 (78)	109
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 6 h	 **I** +  **II** **I** + **II** (79), **I**:**II** = 15:1	108
200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 1.5 h	 **I** +  **II** (40) **I**:**II** = 14:1	108

 400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 12 h	 (100) (*E*)/(*Z*) = 5.7:1	110
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 6 h	 **I** + **II** (65), **I**:**II** = 3.5:1	108
 400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 12 h	 (88) (*E*)/(*Z*) = 5.7:1	110
 200% **I**		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 20 h		108

I (*E*)/(*Z*)	**II** + **III**	**II**:**III**	**III** (*E*)/(*Z*)
80:20	(82)	1:2.5	8.3:1
>97:3	(82)	1:2.5	8.4:1
<4:96	(79)	1.2.5	8.4:1

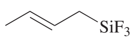
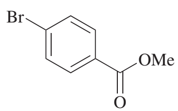
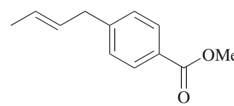
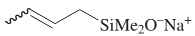
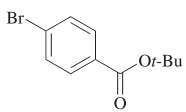
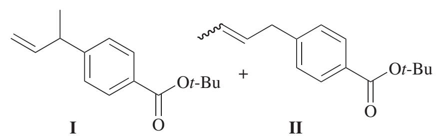
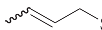
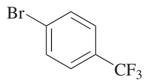
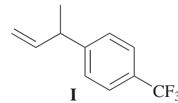
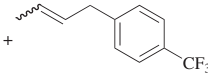
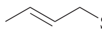
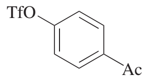
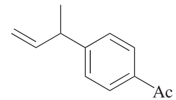
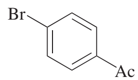
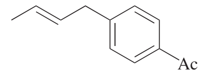
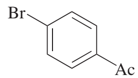
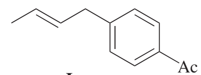
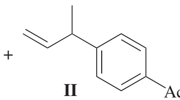
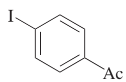
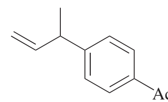
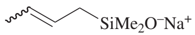
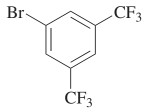
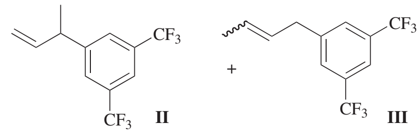
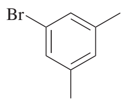
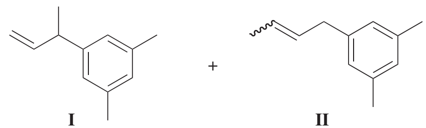
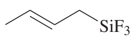
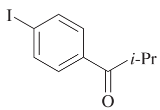
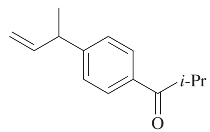
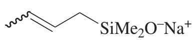
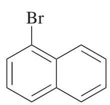
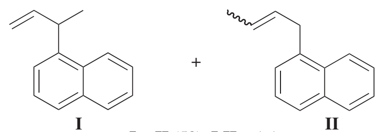
 400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 12 h	 (95) (*E*)/(*Z*) = 7.2:1	110
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 20 h	 **I** + **II** (67), **I**:**II** = 25:1	108

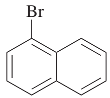
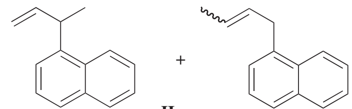
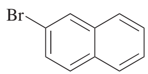
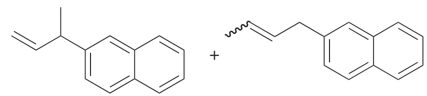
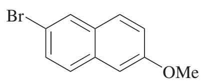
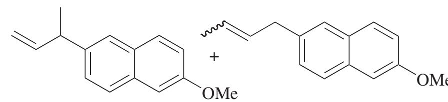
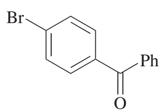
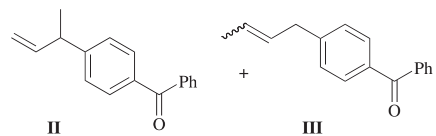
TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 $SiMe_2O^-Na^+$ 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 4 h	 **I** +  **II** **I** + **II** (65), **I**:**II** = 12:1	108
 SiF_3 150%		$Pd(OAc)_2$ (5%), dppb (10%), TASF (100%), THF, 100°	 (96)	109
400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 12 h	 (92) (*E*)/(*Z*) = 7.2:1	110
400%		$PdCl_2$ (5%), **L** (5%), TBAF (300%), THF, 120°	 **I** +  **II**	110
150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 80°	 (95)	109

L	**I** + **II**	**I**:**II**	**I** (*E*)/(*Z*)
$Ph_2PCH_2PPh_2$	(85)	55:45	4.6:1
$Ph_2P(CH_2)_2PPh_2$	(86)	97:1	8.1:1
$Ph_2P(CH_2)_3PPh_2$	(92)	99:1	7.2:1
$Ph_2P(CH_2)_4PPh_2$	(57)	16:1	4.3:1
$Ph_2P(CH_2)_5PPh_2$	(77)	6:94	4.8:1
Ph_3P	(97)	0:100	—

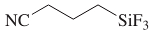
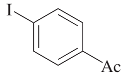
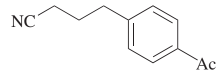
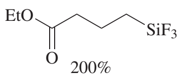
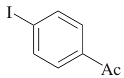
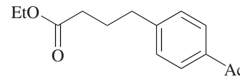
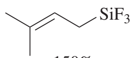
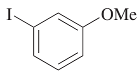
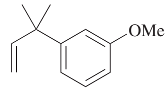
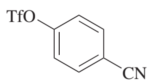
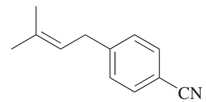
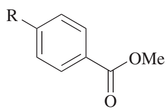
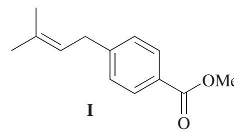
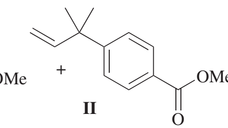
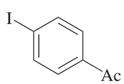
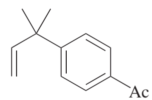
 200% **I**		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 3 h		108
200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 6 h	 **I** + **II** (69), **I**:**II** = 21:1	108
 150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 100°, 90 h	 (95)	109
 250%		$[allylPdCl_2]_2$ (2.5%), Ph_3PO (5%), DME, 85°, 1 h	 **I** + **II** (58), **I**:**II** = 1:1	108

I (*E*)/(*Z*)	**II** + **III**	**II**:**III**
80:20	(62)	3.4:1
>97:3	(74)	3.6:1
<4:96	(68)	2.6:1

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
 200% **I**		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 6 h	 **II** + **III**	108
			I (*E*)/(*Z*) / **II** + **III** / **II**:**III**: 80:20 (50) 14:1; >97:3 (51) 25:1; <4:96 (51) 13:1	
200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 6 h	 **I** + **II**; **I** + **II** (80), **I**:**II** = 25:1	108
200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 3 h	 **I** + **II**; **I** + **II** (69), **I**:**II** = 24:1	108
200% **I**		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 20 h	 **II** + **III**	108
			I (*E*)/(*Z*) / **I** + **II** / **II**:**III**: 80:20 (81) 14:1; >97:3 (79) 24:1; <4:96 (82) 11:1	

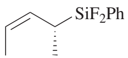
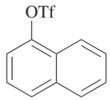
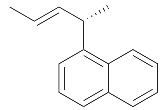
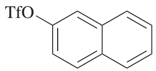
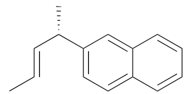
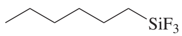
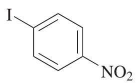
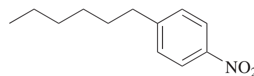
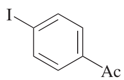
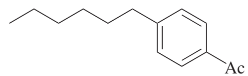
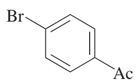
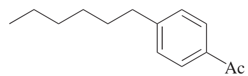
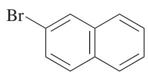
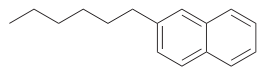
I (*E*)/(*Z*)	**II** + **III**	**II**:**III**
80:20	(50)	14:1
>97:3	(51)	25:1
<4:96	(51)	13:1

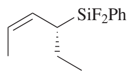
I (*E*)/(*Z*)	**I** + **II**	**II**:**III**
80:20	(81)	14:1
>97:3	(79)	24:1
<4:96	(82)	11:1

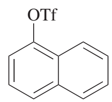
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 24 h	 (86)	190
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 22 h	 (45)	190
C_5				
 150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 100°	 (51)	109
400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°, 48 h	 (49)	110
400%		$PdCl_2(Ph_2P(CH_2)_3PPh_2)$ (5%), TBAF (300%), THF, 120°	 **I** +  **II**	110
150%		$Pd(PPh_3)_4$ (5%), TBAF (300%), THF, 100°	 (70)	109

R	**I + II**	**I:II**
OTf	(60)	100:0
Br	(38)	1:1
I	(35)	73:27

TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES (*Continued*)

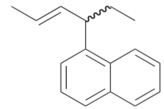
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	 120%	$Pd(Ph_3P)_4$ (4.3%), TASF (400%), DMF, 60°	 (39), er = 79.5:20.5, (*E*)/(*Z*) = 3.1:1	115
	 120%	$Pd(Ph_3P)_4$ (5%), TASF (400%), solvent, 60°	 Solvent / er / (*E*)/(*Z*) THF (64) 70.5:29.5 4.4:1 DMF (70) 83:17 8.6:1	115
C_6				
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 38 h	 (62)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 24 h	 (61)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 37 h	 (63)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 24 h	 (62)	190





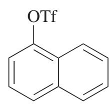
120%

$Pd(Ph_3P)_4$ (4.3%), F^- (400%), solvent, 60°



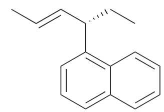
115

F^-	Solvent		er		(*E*)/(*Z*)
TASF	THF	(50)	76.5:23.5	*S*	9.3:1
TASF	DMF	(64)	81.5:18.5	*S*	24:1
CsF	THF	(50)	75.5:24.5	*R*	42:2
CsF	DMF	(50)	81:19	*S*	15:1
KF	THF	(50)	55:45	*R*	100:0
CsF/18-crown-6	THF	(38)	56.5:43.5	*S*	16:1



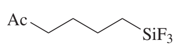
120%

$Pd(Ph_3P)_4$ (4.3%), TASF (400%), solvent, 60°

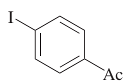


115

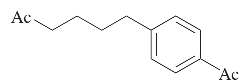
Solvent		er	(*E*)/(*Z*)
THF	(68)	70:30	4.5:1
DMF	(55)	83.5:16.5	4.3:1



200%

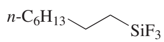


$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 18 h

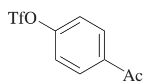


(66) 190

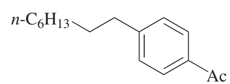
C_8



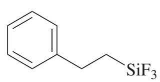
200%



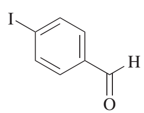
$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 50°, 2.5 h



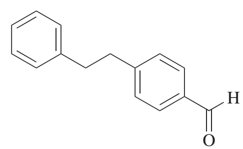
(65) 181



200%



$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 24 h



(61) 190

TABLE 5A. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ARYL ELECTROPHILES (*Continued*)

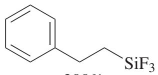
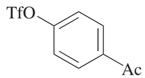
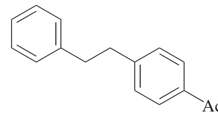
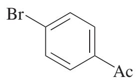
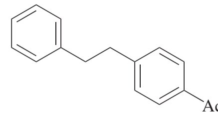
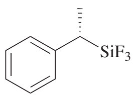
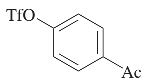
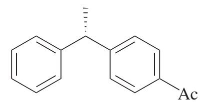
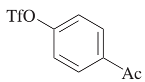
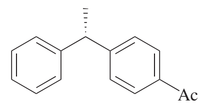
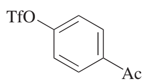
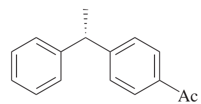
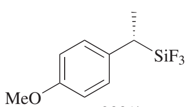
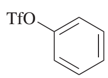
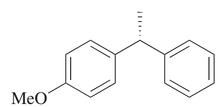
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_8					
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 50°, 2.5 h		(71)	181
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 100°, 34 h		(71)	190
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), solvent, 60°		Solvent — er HMPA/THF (1:10) 54:46 (*R*) DMF/THF (1:10) 58:42 (*S*) DMSO/THF (1:10) 58:42 (*S*)	117
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), solvent, 60°		Solvent — er HMPA/THF (1:10) 54:46 (*R*) DMF/THF (1:10) 58:42 (*S*) DMSO/THF (1:10) 58:42 (*S*)	117
200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 50°		(31–51), er = 66:34–67:33	117
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (200%), THF, 60°		(35), er = 54.5:44.5	117

TABLE 5B. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH HETEROARYL ELECTROPHILES

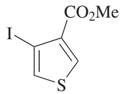
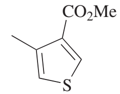
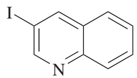
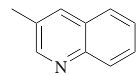
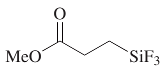
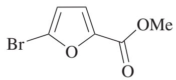
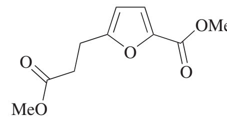
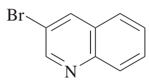
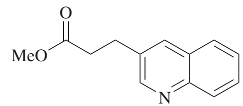
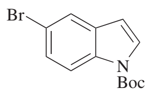
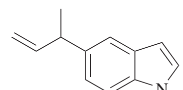
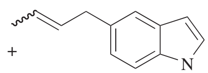
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_1					
$(Et_2N)_3S^+\ Me_3SiF_2^-$ 150%		$[allylPdCl]_2$ (2.5%), DMF, 80°, 24 h		(79)	275
150%		$[allylPdCl]_2$ (2.5%), DMF, 80°, 24 h		(66)	275
C_3					
 200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 48 h		(36)	190
200%		$Pd(Ph_3P)_4$ (5%), TBAF (400%), THF, 100°, 8 h		(65)	190
C_4					
 200%		$Pd(dba)_2$ (5%), norbornadiene (5%), toluene, 70°, 3.5 h	 **I** +  **II** **I** + **II** (83), **I**:**II** = 19:1		108

TABLE 5C. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ALKENYL ELECTROPHILES

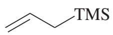
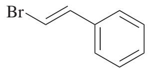
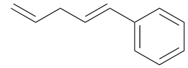
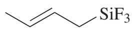
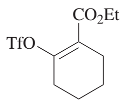
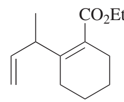
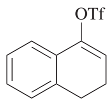
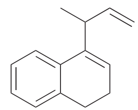
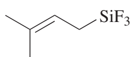
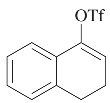
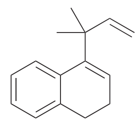
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
 133%		$[allylPdCl]_2$ (2.5%), TASF (133%), THF, rt	 (28)	23
C_4				
 150%		$Pd(OAc)_2$ (5%), dppb (10%), TASF (100%), THF, 120°	 (98)	109
150%		$Pd(OAc)_2$ (5%), dppb (10%), TASF (100%), THF, 100°	 (85)	109
C_5				
 150%		$Pd(OAc)_2$ (5%), dppb (10%), TASF (100%), THF, 120°	 (83)	109

TABLE 5D. CROSS-COUPLING OF sp^3-ORGANOSILANES WITH ALKYL ELECTROPHILES

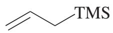
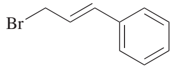
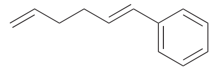
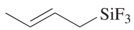
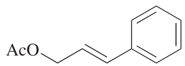
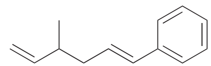
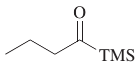
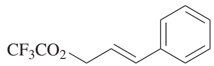
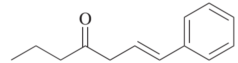
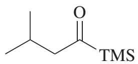
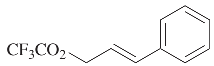
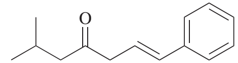
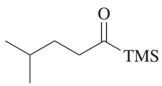
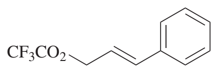
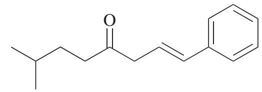
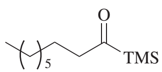
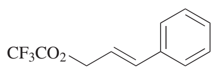
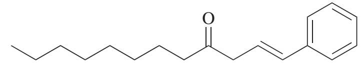
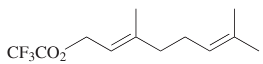
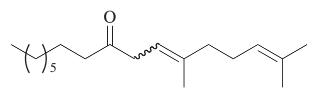
Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_3					
 133%		$[allylPdCl]_2$ (5%), TASF (133%), THF, rt		(83)	23
C_4					
 150%		$Pd(PPh_3)_4$ (5%), TBAF (150%), THF, 60°		(54)	109

TABLE 6. CROSS-COUPLING OF ACYL ORGANOSILANES WITH ALLYL ELECTROPHILES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (55)	148
C_5				
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (43)	148
C_6				
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (56)	148
C_9				
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (63)	148
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (60), (*E*)/(*Z*) = 68:32	148

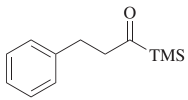
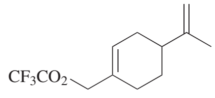
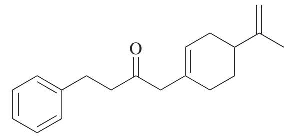
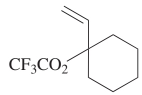
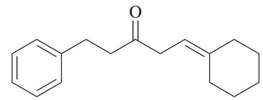
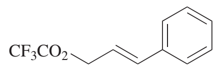
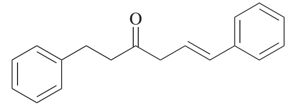
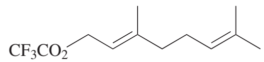
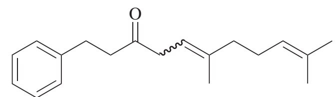
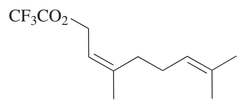
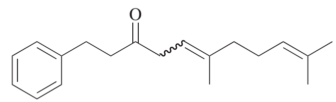
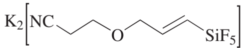
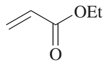
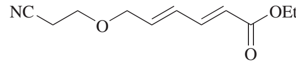
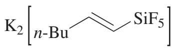
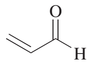
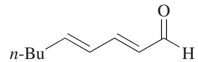
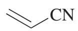
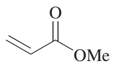
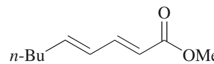
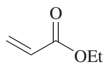
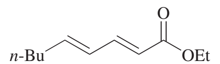
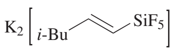
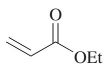
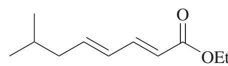
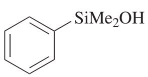
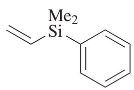
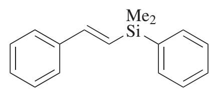
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h		(36)	148
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h		(46)	148
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h		(60)	148
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (58), (*E*)/(*Z*) = 71:29		148
	 200%	Pd cat. **6** (5%), THF, reflux, 16 h	 (44), (*E*)/(*Z*) = 63:37		148

TABLE 7. OXIDATIVE HECK REACTION OF ALKENYL- AND ARYLSILANES

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 20 h	 (23)	21
C_6				
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 4 h	 (20)	21
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 45 h	 (43)	21
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 47 h	 (37)	21
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 20 h	 (48)	21
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 20 h	 (38)	21
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h	 (57)	277

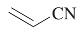
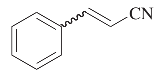
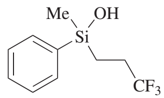
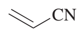
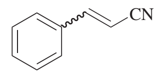
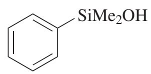
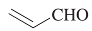
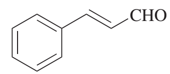
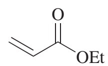
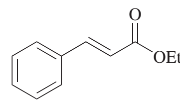
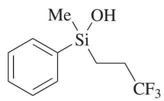
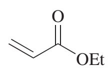
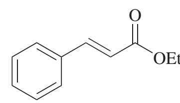
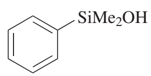
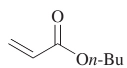
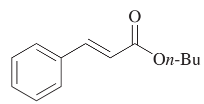
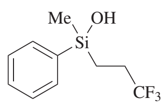
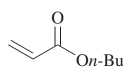
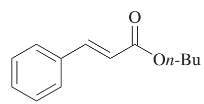
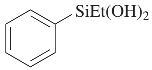
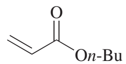
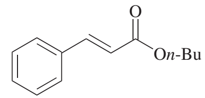
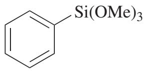
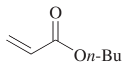
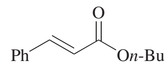
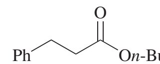
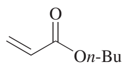
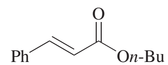
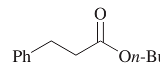
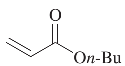
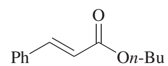
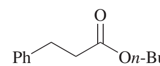
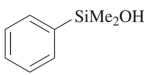
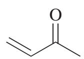
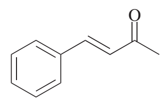
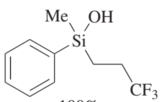
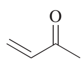
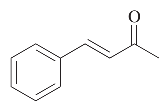
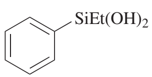
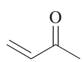
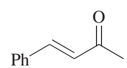
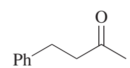
100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(34) (*E*)/(*Z*) ~ 2:1	277
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 3 h		(43) (*E*)/(*Z*) ~ 5:2	203
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(37)	277
100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(56)	277
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 3 h		(70)	203
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(69)	277
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, rt, 48 h		(57)	277

TABLE 7. OXIDATIVE HECK REACTION OF ALKENYL- AND ARYLSILANES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 300%	$[Ir(OMe)(cod)]_2$ (3%), toluene, 120°, 24 h	 (64)	279
	 300%	$[IrCl(cod)]_2$ (5%), TBAF (100%), toluene/H_2O (6:1), 120°, 24 h	 (71) +  (0)	279
	 300%	$[IrCl(cod)]_2$ (5%), TBAF (100%), toluene/H_2O (6:1), 70°, 24 h	 (62) +  (3)	279
	 300%	$[IrCl(cod)]_2$ (5%), TBAF (100%), toluene/H_2O (6:1), 120°, 24 h	 (70) +  (5)	279
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h	 (48)	277
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 3 h	 (79)	203
	 300%	$[Ir(OMe)(cod)]_2$ (3%), toluene, 120°, 24 h	 (50) +  (4)	279

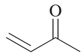
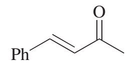
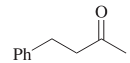
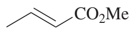
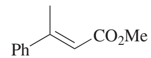
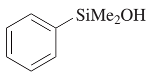
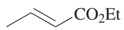
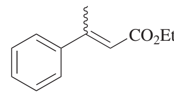
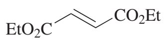
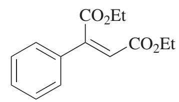
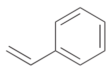
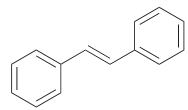
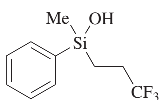
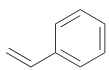
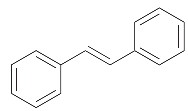
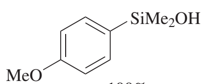
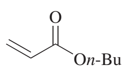
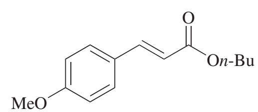
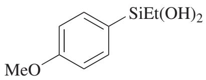
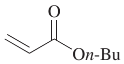
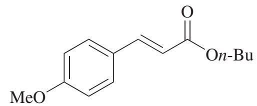
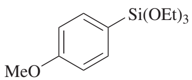
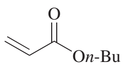
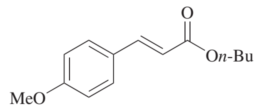
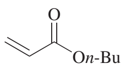
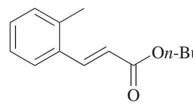
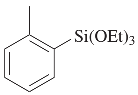
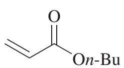
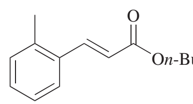
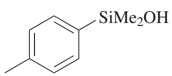
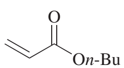
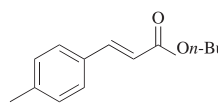
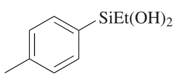
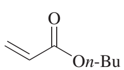
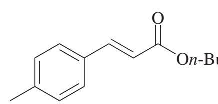
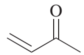
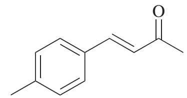
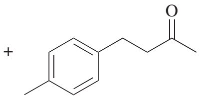
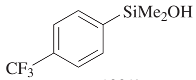
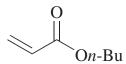
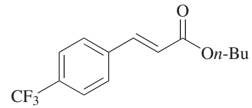
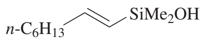
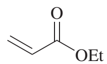
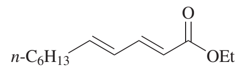
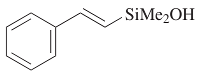
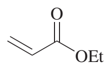
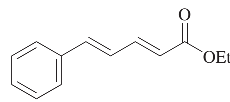
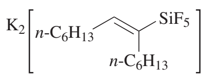
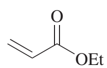
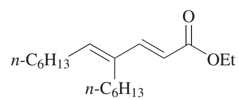
	 300%	$[Ir(OMe)(cod)]_2$ (3%), toluene/H_2O (6:1), 120°, 24 h	 (41) +  (8)		279
$K_2[PhSiF_5]$	 1000%	$Pd(OAc)_2$ (100%), MeCN, reflux, 32 h		(53)	21
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 48 h		(55) (*E*)/(*Z*) ~ 9:1	277
100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 48 h		(49)	277
100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(63)	277
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 3 h		(59)	203
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(55)	277

TABLE 7. OXIDATIVE HECK REACTION OF ALKENYL- AND ARYLSILANES (*Continued*)

Silane	Electrophile	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6					
	 300%	$[Ir(OMe)(cod)]_2$ (5%), toluene/H_2O (6:1), 120°, 24 h		(62)	279
	 300%	$[IrCl(cod)]_2$ (5%), TBAF (100%), THF/H_2O (6:1), 70°, 24 h		(70)	279
C_7					
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(54)	277
	 300%	$[Ir(OMe)(cod)]_2$ (7.5%), TBAF (100%), toluene/H_2O (6:1), 70°, 24 h		(61)	279
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h		(54)	277
	 300%	$[Ir(OMe)(cod)]_2$ (5%), toluene/H_2O (6:1), 120°, 24 h		(63)	279

	 300%	$[Ir(OMe)(cod)]_2$ (3%), toluene/H_2O (6:1), 120°, 24 h	 (52) +  (8)	279
 100%		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (100%), LiOAc (200%), DMF, 100°, 24 h	 (65)	277
C_8				
		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 44 h	 (52)	277, 278
		$Pd(OAc)_2$ (10%), $Cu(OAc)_2$ (300%), LiOAc (200%), DMF, 100°, 44 h	 (41)	277, 278
C_{14}				
	 1000%	$Pd(OAc)_2$ (100%), THF, rt, 48 h	 (28)	21

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CHAPTER 4

THE AZA-COPE/MANNICH REACTION

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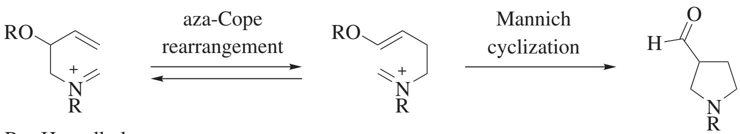
INTRODUCTION

Because of their ability to rapidly build molecular complexity, reactions that construct several carbon–carbon bonds are of special value in organic synthesis. Among these transformations, cascade reactions form several bonds by an orchestrated sequence in which the first bond-forming step reveals functionality that allows a subsequent bond-forming transformation.[1–3] In 1979, such a sequence for the synthesis of 3-acylpyrrolidines and azacyclic structures that contain this unit was first reported (Eq. 1).[4] In this reaction, now commonly

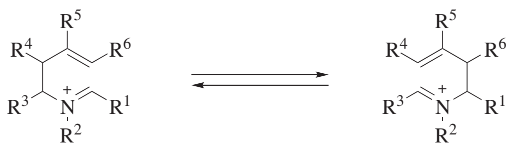
referred to as the aza-Cope/Mannich reaction, a [3,3]-sigmatropic rearrangement of an unsaturated iminium cation generates the iminium ion and enol (or enol ether) that are the participants in a subsequent intramolecular Mannich reaction.



R = H or alkyl

(Eq. 1)

This pyrrolidine synthesis exploits the ability of a positively charged nitrogen atom to decrease the activation barrier of the [3,3]-sigmatropic reorganization.[5] Cationic aza-Cope rearrangements, alternatively termed 2-azonia-[3,3]-sigmatropic rearrangements (Eq. 2), take place at temperatures 100–200° lower than [3,3]-sigmatropic rearrangements of hydrocarbon counterparts.[6–8] Although the process has never been analyzed in detail, factors that likely contribute to this significant rate acceleration have been discussed.[9] To be of use in synthesis, cationic aza-Cope rearrangements must produce largely one constitutional isomer. Prior to the introduction of the cascade reaction that is the subject of this chapter, applications of cationic aza-Cope rearrangements in synthesis were limited to substrates wherein the sigmatropic rearrangement was rendered irreversible by ring strain[10–12] or aryl conjugation (**1** → **2**, R^3 = aryl) of the iminium ion product.[13–17] No such limitation exists in the aza-Cope/Mannich reaction, as less stable iminium ion isomers are readily trapped by exothermic intramolecular Mannich reactions.



1 **2**

(Eq. 2)

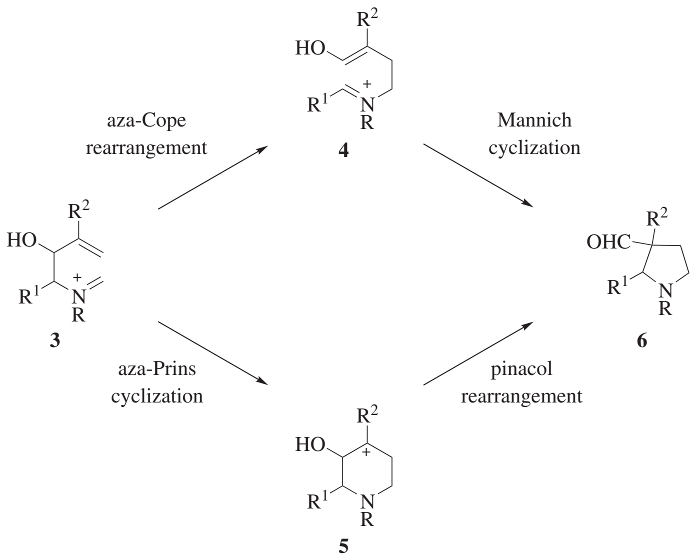
The aza-Cope/Mannich reaction has not been the subject of a comprehensive review, although aspects of the reaction have been discussed in several more general summaries.[7–9,18–21] The present chapter covers the common version of the transformation depicted in Eq. 1, along with the formation of 3-acylpyrrolidines by a related base-promoted cascade sequence. Coverage is limited to reactions that take place in one operation. Related cascade reactions that form different pyrrolidine products, such as aza-Cope rearrangement/aza-Prins cyclization sequences,[22–24] are also excluded from the present chapter.

MECHANISM AND STEREOCHEMISTRY

Mechanism

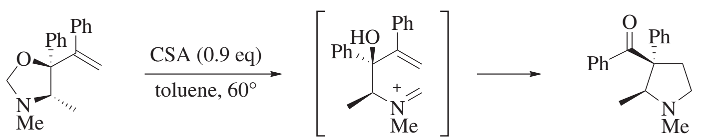
Several mechanisms have been considered for the aza-Cope/Mannich reaction. In addition to the aza-Cope/Mannich sequence (**3** → **4** → **6**), the transformation

of an iminium cation **3** into a 3-acylpyrrolidine **6** could take place by a two-step process involving initial aza-Prins cyclization to form a 4-piperidinyl carbenium ion **5**, followed by pinacol rearrangement of this intermediate (Scheme 1). In the most common variant wherein the iminium cation is *N*-unsubstituted or *N*-alkyl substituted, the aza-Cope/Mannich mechanism is believed to be generally operative.



Scheme 1

Investigation of the fate of a chiral, enantiomerically enriched iminium ion substrate allows a distinction between these mechanisms to be made: a cyclization/pinacol mechanism should occur with retention of configuration at the carbon bearing the R^1 substituent of **3**, whereas the aza-Cope/Mannich mechanism could produce racemic products as intermediate **4** is achiral. In a key test, oxazolidine **7** (90% ee) is transformed into racemic 3-acylpyrrolidine **8** when heated at 60° in the presence of 0.9 equivalents of camphorsulfonic acid (CSA) (Eq. 3). Control experiments confirm that an enantiomerically enriched sample of pyrrolidine **8** undergoes only slight racemization under these reaction conditions. These results provide strong support for the aza-Cope/Mannich mechanism.[25]

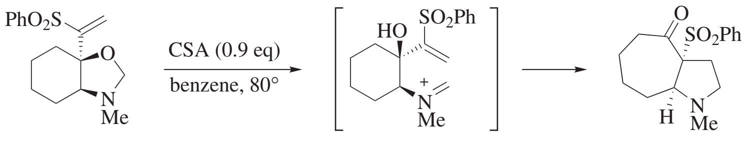


(Eq. 3)

7 (90% ee) **8** (79%) racemic

Another observation in accord with the aza-Cope/Mannich mechanism for reactions of simple iminium ions is the successful synthesis of 3-acylpyrrolidines

with substrates containing a variety of substituents at the internal alkene carbon (R^2). One would expect an aza-Prins cyclization/pinacol rearrangement sequence to be highly sensitive to the nature of the R^2 substituent, as this substituent interacts directly with the carbenium carbon of piperidinyl cation **5** (Scheme 1). In one study, substituents at this position were varied widely (OEt, SPh, Me, H, SO_2Ph) to represent extremes of $>10^{17}$ in their abilities to stabilize a positive charge.[25] The successful transformation of substrate **9** containing the strongly electron-withdrawing sulfone substituent to acylpyrrolidine **10** provides additional evidence for the aza-Cope/Mannich mechanism (Eq. 4).



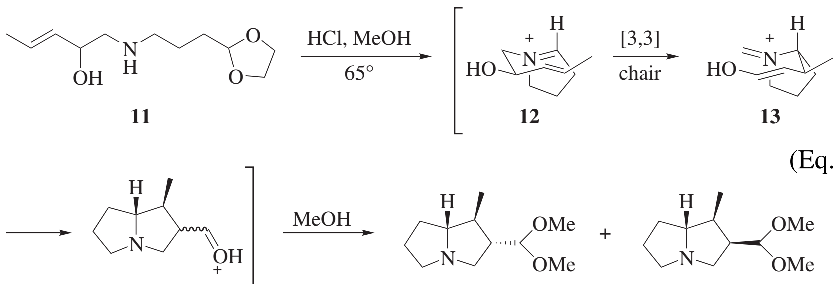
(Eq. 4)

9 **10** (85%)

Increasing the nucleophilicity of the alkene or the electrophilicity of the iminium cation should favor an aza-Prins/pinacol mechanism. This mechanistic alternative has been suggested for syntheses of 3-acylpyrrolidines in which the alkene is an enol ether,[25] or the electrophile is a strongly electrophilic *N*-sulfonyliminium cation.[26,27]

Stereochemistry

The iminium cation intermediate produced in the sigmatropic rearrangement step of most aza-Cope/Mannich reactions contains one or more stereogenic carbons. Thus, one feature that critically influences stereochemical transfer is the geometry of the sigmatropic rearrangement step. A great deal of evidence indicates that this step takes place preferentially via a chair-like transition structure. For example, exposure of (E)-amino alcohol acetal **11** to 1.2 equivalents of HCl in MeOH at 65° produces pyrrolizidine acetals **14** and **15** in a combined yield of 90% (Eq. 5).[28] The *cis*-relationship of the methyl substituent and the angular hydrogen in these products signals that the [3,3]-sigmatropic rearrangement step (**12** → **13**) occurs by a chair geometry.



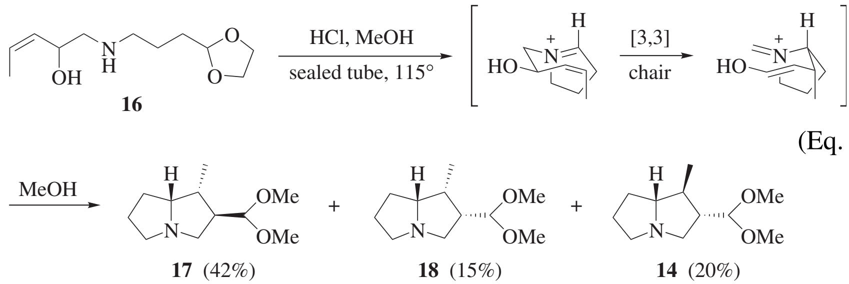
11 **12** **13**

(Eq. 5)

14 (84%) **15** (6%)

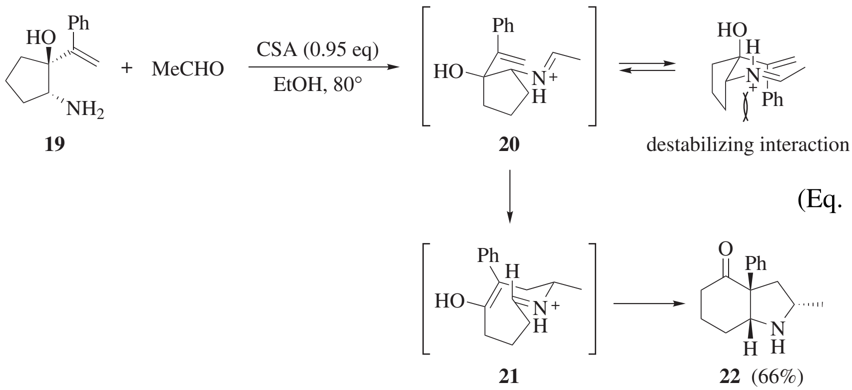
A preference for the aza-Cope rearrangement to occur via a chair conformation is also seen in the related transformation of (Z)-amino alcohol acetal **16** to give

predominantly pyrrolizidine acetal products **17** and **18** having a *trans* relationship of the methyl substituent and the angular hydrogen (Eq. 6).[28] However, in this case the chair/boat preference is much less (3:1) than that observed with E-substrate **11** (chair/boat >90:1). The lower chair selectivity with the (Z)-alkene substrate is attributed to steric interactions between the (Z)-methyl substituent and the five-membered ring. Consistent with the destabilizing nature of this interaction and the sigmatropic rearrangement being at least partially rate-limiting, the aza-Cope/Mannich transformation of Z-substrate **16** requires a reaction temperature that is 50° higher than that required to transform E-substrate **11** under identical conditions.



(Eq. 6)

A preference for the cationic aza-Cope rearrangement to take place via a chair geometry rationalizes the stereoselection that is observed in most aza-Cope/Mannich reactions. Although this aspect of the reaction will be discussed in more detail in a later section, an additional illustrative example is shown below. Thus, acid-promoted condensation of *trans*-2-amino-1-(1-ethenyl)cyclopentanol **19** with acetaldehyde delivers *cis*-hydroindolone **22** as the exclusive product of this ring-enlarging pyrrolidine annulation (Eq. 7).[29] In this case, two chair geometry transition structures exist by which the aza-Cope rearrangement can take place. Of these, the rearrangement via chair conformer **20** should be favored because the alternate chair conformation experiences a quasi-1,3-diaxial interaction between the phenyl substituent and the C3 carbon of the cyclopentane ring.



(Eq. 7)

For the geometry of the sigmatropic rearrangement step to dictate the stereochemical outcome of an aza-Cope/Mannich reaction, the intramolecular Mannich cyclization must take place more rapidly than any stereomutation of the product iminium ion. In the reaction described in Eq. 7, the intramolecular Mannich cyclization of *cis,trans*-azacyclononadiene intermediate **21** must be faster than a change in configuration of the enol or iminium ion π-bonds, which could occur by either enol/keto or iminium ion/enamine tautomerization. Implicit in the stereochemical analysis depicted in Eq. 7 is the expectation that the (E)-iminium ion stereoisomer generated from acid-promoted condensation of amine **19** with acetaldehyde should preferentially undergo sigmatropic rearrangement; it is both more stable than its Z-stereoisomer and its sigmatropic rearrangement places the methyl substituent in a favored equatorial orientation in a chair transition structure.

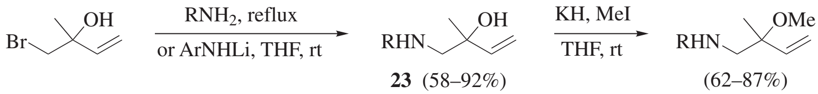
The preference for aza-Cope rearrangements to occur via chair geometries appears to be greater than that of the corresponding Cope rearrangements of hydrocarbons. Thus, the thermal rearrangement of *cis*-1,2-divinylcyclopentane, the hydrocarbon analog of the sigmatropic rearrangement step shown in Eq. 7, occurs preferentially in a boat geometry.[30] However, a boat rearrangement process for the conversion of amino alcohol **19** into hydroindolone **22** can be ruled out. Such a boat transition structure would orient the methyl group of (E)-iminium ion intermediate **20** *syn* to the phenyl substituent, and lead to the unobserved methyl epimer of product **22**.

SCOPE AND LIMITATIONS

Preparation of 1-Aminobut-3-en-2-ols

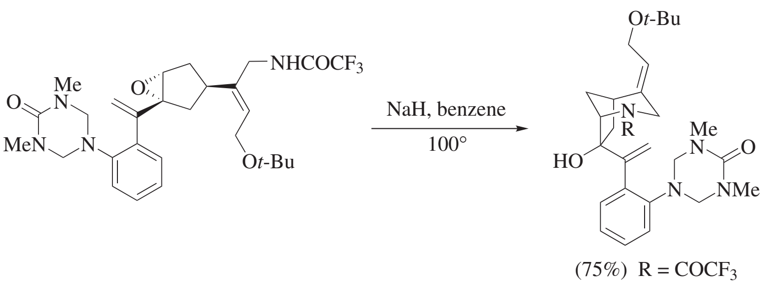
The ease of synthesis of the 1-aminobut-3-en-2-ol precursors for the aza-Cope/Mannich reaction has contributed to its widespread use in synthesis. Although many methods are available for the construction of such amino alcohols, this section focuses on those methods actually used to assemble substrates for aza-Cope/Mannich reactions.

Epoxide Ring Opening. The preference for many terminal epoxides to undergo a site-selective bimolecular ring opening with amine nucleophiles has allowed the large-scale synthesis of a number of 1-aminobut-3-en-2-ols. For example, treatment of isoprene oxide (generated in situ from 1-bromo-2-methyl-3-buten-2-ol) with 1.3 equivalents of a primary aliphatic amine gives 2-methyl-1-(alkylamino)-3-buten-2-ols **23** in moderate to good yields (58–92%) (Eq. 8).[4,31] Aromatic amines can also be used, although lithium anilides, typically generated by reaction with n-butyllithium, are found to be more effective nucleophiles in such cases. Selective O-methylation of these adducts is achieved in good yield by reaction of the amino alcohol products with one equivalent of potassium hydride and one equivalent of methyl iodide. It is of note that the reaction of n-propylamine with butadiene oxide is much less selective, giving a 2.6:1 mixture of constitutionally isomeric products.[31]



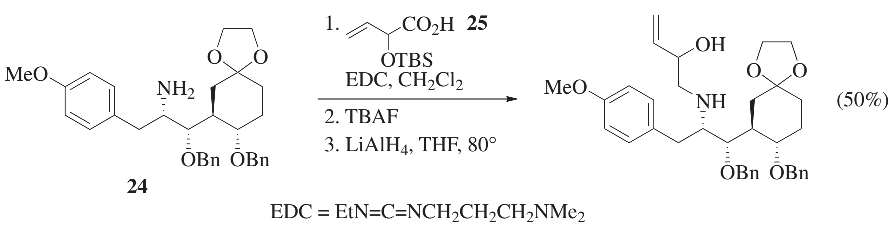
(Eq. 8)

Intramolecular epoxide ring opening has also been used to access a number of 1-aminobut-3-en-2-ols. For example, intramolecular 6-exo epoxide ring opening with the sodium salt of a trifluoroacetyl-substituted amine is used to access a tetracyclic intermediate containing a 1-aminobut-3-en-2-ol fragment during the asymmetric total synthesis of the Wieland-Gumlich aldehyde and (−)-strychnine (Eq. 9).[32,33] In this and several related cases,[34−38] the alkene portion of the vinyl epoxide is introduced conveniently by Wittig olefination of the corresponding ketone.



(Eq. 9)

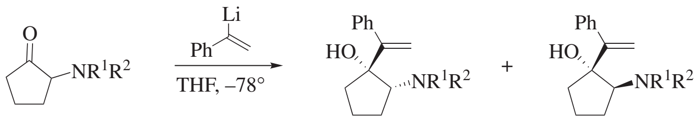
Amine Alkylation. Reaction of an amine with 4-bromo-3-methoxy-1-butene has also been employed to prepare 1-amino-3-buten-2-ols, although over-alkylation is a frequently encountered problem,[4,31,39,40] even under conditions specifically designed to favor mono-alkylation.[39] To overcome this issue, reductive amination is used on occasion;[41] however, amide bond formation, followed by carbonyl reduction is used more frequently.[28] In the example illustrated in Eq. 10,[40] carbodiimide-mediated coupling between amine **24** and carboxylic acid **25** generates an amide, which after desilylation and reduction with $LiAlH_4$ gives the precursor of an aza-Cope/Mannich reaction.



(Eq. 10)

Vinylation of α-Amino Aldehydes or Ketones. Forming the 1-amino-3-buten-2-ol fragment by vinylation of an α-amino carbonyl compound offers the opportunity to control the relative configuration of the amino and vinyl groups.[42−45] Typically a lithium reagent is used, but cerium reagents are reported

in some cases to be superior.[44–46] The nature of the nitrogen substituent has a profound effect on the diastereoselectivity of nucleophilic addition to cyclic α-amino ketones: dimethyl substitution or a cyanomethyl-benzyl substituent combination allows a highly diastereoselective synthesis of the *anti* product (9:1 *anti*/*syn*), whereas a benzophenone imine derivative gives a 2:1 mixture favoring addition *syn* to the imine (Eq. 11).[29] Presumably, the reversal in selectivity seen with imine substitution reflects coordination of the lithium reagent with the imine nitrogen.

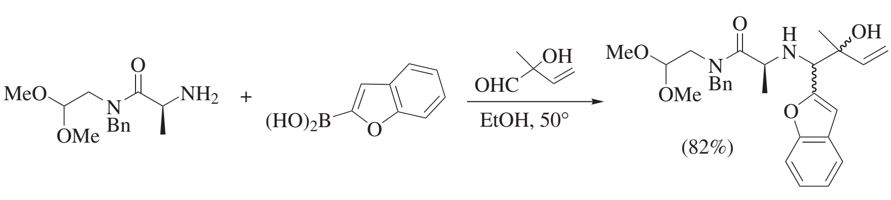


(Eq. 11)

$R^1 = CH_2CN$, $R^2 = Bn$	(74%)	(8%)
R^1, $R^2 = Me$	(54%)	(5%)
R^1, $R^2 = Ph_2C=$	(30%)	(55%)

Incorporation of a cyanomethyl group into an aza-Cope/Mannich synthetic sequence can serve a dual purpose: not only can it protect the basic nitrogen and facilitate the stereoselective synthesis of the required precursor, it can also serve as a masked formaldiminium ion intermediate, a feature that will be discussed later. It should be noted that at temperatures above −78°, the cyanomethyl group is reactive with a vinyllithium species, so cryogenic temperatures should be maintained throughout the reaction and quenching.[47,48] High levels of diastereoselectivity with cyanomethyl-alkyl protection are reported for cyclic α-keto amines derived from cyclobutanone,[49] cyclopentanone, and cyclohexanone.[50]

Other methods that are used for the synthesis of 1-aminobut-3-en-2-ol precursors for the aza-Cope/Mannich reaction include the Petasis reaction (Eq. 12),[51] *E*-selective reduction of 1-aminobut-3-yne-2-ols with $LiAlH_4$,[52] and Curtius rearrangement of 3-hydroxy-4-pentenoic acids.[53]



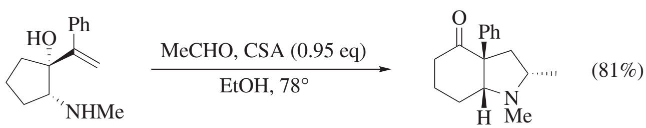
(Eq. 12)

In much of the early development of the aza-Cope/Mannich reaction, amino alcohol intermediates were prepared as racemates. However, as will be discussed shortly, because of the high levels of diastereoselectivity in the aza-Cope/Mannich reaction, preparation of an enantiopure 1-aminobut-3-en-2-ol precursor typically results in the formation of an enantiopure 3-acylpyrrolidine product. Many enantioselective methods developed in recent years for preparing allylic alcohols can

now be utilized to prepare a variety of precursors containing the 1-aminobut-3-en-2-ol unit as a single enantiomer.[54]

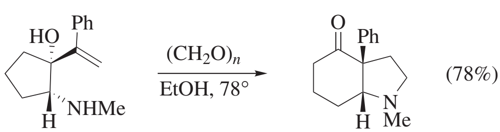
Iminium Ion Generation

From Condensation of Amine and Carbonyl Precursors. Although several methods exist for generation of an iminium ion from substrates containing the 1-aminobut-3-en-2-ol functional group array, the most commonly used method is acid-mediated condensation with one equivalent of an aldehyde (Eq. 13).[29,55] A variety of solvents can be used for this condensation reaction, typically benzene, acetonitrile, or ethanol, although toluene, tetrahydrofuran, nitromethane, and dimethyl sulfoxide have also been used. The reaction generally uses reflux temperatures with an amine salt or the free amine and less than one equivalent of a sulfonic acid (typically CSA);[31] under these conditions the pH of the reaction is effectively neutral. Non-bulky aldehydes participate readily in aza-Cope/Mannich reactions, including sensitive aldehydes such as cinnamaldehyde, ethyl glyoxylate, furfural, and citral.[31,56] When glyoxylic acid is used, no external acid is required for the aza-Cope/Mannich reaction.[57] Examples exist of iminium ion generation by condensation of 1-aminobut-3-en-2-ols with aldehydes using microwave irradiation, or in the presence of one equivalent of CSA and copper sulfate; these conditions are reported to decrease reaction times for the aza-Cope/Mannich reaction.[56]



(Eq. 13)

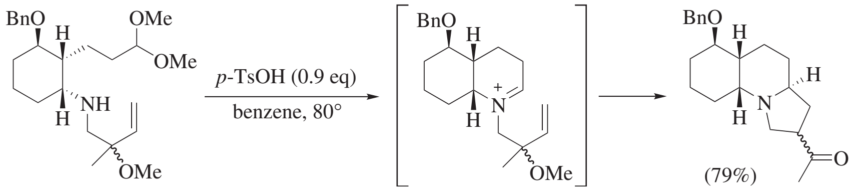
When formaldehyde is used, the anhydrous monomeric form of formaldehyde does not need to be generated; commercially available, solid paraformaldehyde typically works well for iminium ion formation.[31] Typically, less than one equivalent of CSA is added to mediate iminium ion generation,[44,45] often in the presence of sodium sulfate. In some cases, the trace of formic acid present in paraformaldehyde is sufficient to catalyze iminium ion generation and the subsequent aza-Cope/Mannich reaction (Eq. 14).[58]



(Eq. 14)

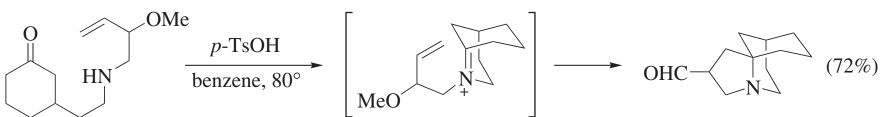
Intramolecular condensation with a tethered aldehyde has been used sparingly, although iminium ions suitable for the aza-Cope/Mannich reaction can be accessed in this manner.[28] Typically, the carbonyl group is protected as the

dimethyl acetal, with iminium ion formation occurring directly from this precursor (Eq. 15).[41]



(Eq. 15)

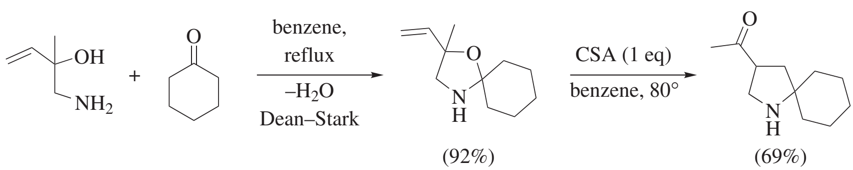
Although simple aldehydes are useful for direct iminium ion generation by intermolecular condensation, similar reactions with bulky aldehydes or ketones are typically unsuccessful.[31,59] As discussed in more detail below, this limitation is readily overcome by first generating an oxazolidine intermediate. Despite failures with intermolecular condensation of amines with ketones, intramolecular condensations can be successful. For example, bridgehead iminium ion **26** is generated by intramolecular amine–ketone condensation in the presence of *p*-toluenesulfonic acid in refluxing benzene and undergoes a successful aza-Cope/Mannich reaction (Eq. 16).[39]



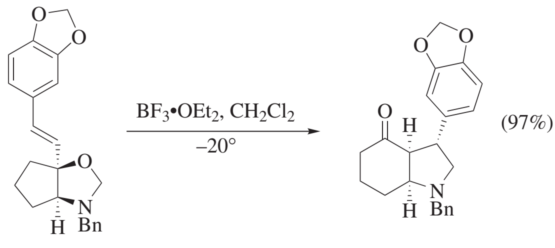
26

(Eq. 16)

From Oxazolidines. As noted previously, bulky aldehydes such as 2,2-dimethylpropanal or ketones do not participate in aza-Cope/Mannich reactions under the same mild conditions as most aldehydes.[31] This limitation is easily overcome by simply generating an oxazolidine intermediate under dehydrating conditions from the carbonyl component and the 1-aminobut-3-en-2-ol substrate. Aza-Cope/Mannich rearrangement is then promoted by heating the oxazolidine intermediate with a stoichiometric amount of a protic acid such as CSA (Eq. 17).[31,59] Lewis acids can also be employed, in some cases with advantage. For example, whereas exposure of oxazolidine **27** to protic acids in a variety of solvents is unsuccessful at generating the aza-Cope/Mannich product, reaction of **27** with 2.4 equivalents of boron trifluoride etherate at −20° allows the desired aza-Cope/Mannich reaction to proceed in 97% yield (Eq. 18).[60] This reaction can also be realized with tin tetrachloride or trimethylsilyl trifluoromethanesulfonate, but conversion to the product is reported to be slower with these Lewis acids.



(Eq. 17)



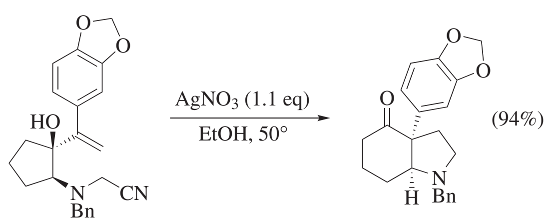
27

(Eq. 18)

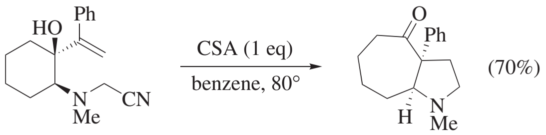
An alkylating agent can also be used to generate an iminium ion from an oxazolidine precursor. However, mixtures of alkylated and non-alkylated pyrrolidines are typically formed.[31] Presumably, the acid generated in situ is responsible for catalyzing the background aza-Cope/Mannich reaction of the non-alkylated oxazolidine.

Oxazolidines containing no substituent on nitrogen can also be transformed to aza-Cope/Mannich products under basic conditions.[61,62] This little-developed anionic version of the aza-Cope/Mannich reaction will be discussed in a later section.

From Cyanomethyl Groups. As mentioned previously, a cyanomethyl group can act as a nitrogen-protecting group and also as a precursor of a formaldiminium ion to initiate the aza-Cope/Mannich reaction. A number of silver and copper complexes capable of 'trapping' cyanide are competent at activating a cyanomethyl group on mild heating, including silver nitrate, silver trifluoroacetate, silver acetate, copper trifluoroacetate, and copper triflate (Eq. 19).[29,46,47,50] Typically ethanol is used as the solvent, although chloroform,[50] tetrahydrofuran,[46] or diethyl ether can also be employed.[25] A combination of silver nitrate and pyridine in chloroform can be used if basic conditions are required, although the reaction is slower than with silver nitrate alone.[50] The cyanomethyl group can also be transformed into an iminium ion by treatment with protic acids, but the reaction is typically slower than when Lewis acids are used (Eq. 20).[47] The various choices available for generating a formaldiminium ion from a cyanomethyl group allow a wide selection of reaction conditions for aza-Cope/Mannich reactions initiated in this way.

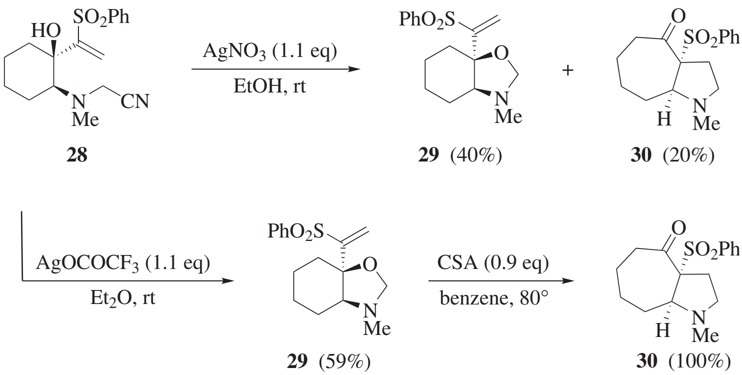


(Eq. 19)



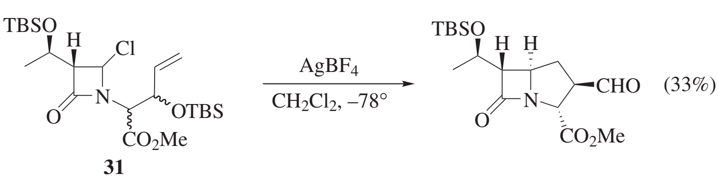
(Eq. 20)

If the alkene of a substrate is a weak nucleophile, initiating an aza-Cope/Mannich reaction from a cyanomethyl group can be problematic. For example, treatment of precursor **28** with silver nitrate gives a 2:1 mixture of oxazolidine **29** and aza-Cope/Mannich product **30** in a combined 60% yield (Scheme 2).[25] However, this problem is overcome by allowing cyanomethyl precursor **28** to react with silver trifluoroacetate in diethyl ether to generate oxazolidine **29**, which on subsequent reaction with 0.9 equivalent of CSA in refluxing benzene gives the aza-Cope/Mannich product, cycloheptapyrrolidine **30**, in quantitative yield.



Scheme 2

Generation of *N*-Acyliminium Ions. The vast majority of aza-Cope/Mannich reactions reported to date involve simple iminium ion intermediates, although related transformations of *N*-acyliminium ions have occasionally been reported.[63,64] For example, chloride elimination from 4-chloroazetidinone **31** on reaction with silver tetrafluoroborate at −78° gives the carbapenam product in 33% yield (Eq. 21).[64] The authors reported the inability to realize the same transformation on reaction of the corresponding 4-acetoxy precursor with various Lewis acids.

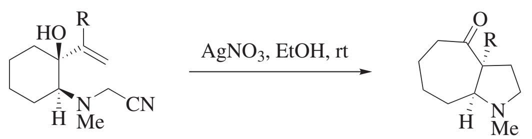


(Eq. 21)

Nature of the Vinyl Substituent

Vinyl groups of differing steric demand and electronic nature are generally compatible with the aza-Cope/Mannich reaction.

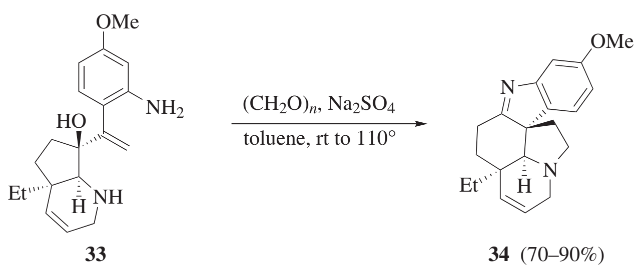
1,1-Disubstitution. In most aza-Cope/Mannich reactions reported to date, the alkene participant bears a single substituent at the internal alkene carbon. Such substrates containing electron-withdrawing and electron-donating alkene substituents covering a $>10^{17}$ range in their ability to stabilize a positive charge are viable substrates for aza-Cope/Mannich reactions (Eq. 22).[25] Of note is the use of silver nitrate buffered with pyridine to prevent epimerization of product **32** when R = H. However, to realize a high yield in the reaction of the precursor containing the strongly electron-withdrawing phenyl sulfonyl group does require more forcing conditions (Scheme 2). The transformation depicted in Eq. 22 is also possible when the alkene is a vinyl ether (R = OEt); however, in this case, cycloheptapyrrolidine **32** (R = OEt) is isolated from a complex mixture in only 37% yield.[25]



(Eq. 22)

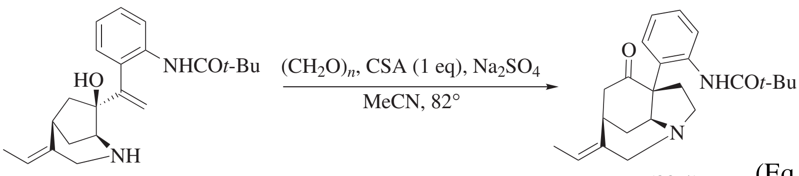
R = H, Me, SPh, SO$_2$Ph, Ph, OEt **32** (59–78%)

Substrates containing aryl substituents of various types at the internal carbon of the alkene have been employed widely. Anilines are tolerated, both unprotected,[36,65] and protected as amides[37,38] or carbamates[38] (Eqs. 23–25). The unprotected aniline group of substrate **33** survives the reaction, and ultimately condenses with the ketone carbonyl group to give pentacyclic imine product **34**. As shown in Eqs. 24 and 25, the pivalamide fragment of precursor **35** does not undergo cyclization with the ketone carbonyl of the aza-Cope/Mannich product, whereas the carbamate-protected aniline substituent in substrate **36** cyclizes to give tetracyclic product **37**. The ready dehydration, following aza-Cope/Mannich reaction, observed in the reaction depicted in Eq. 25 could not be avoided under any experimental conditions.[38]

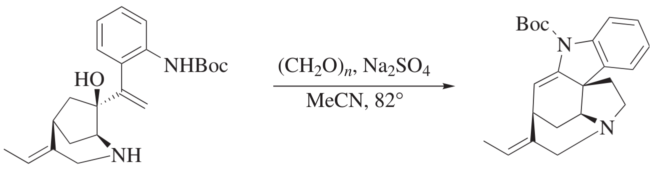


(Eq. 23)

33 **34** (70–90%)

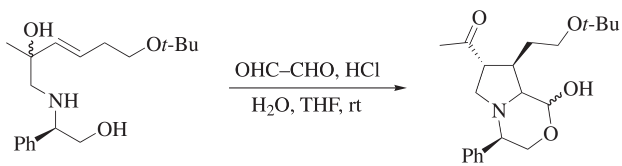


35 (88%) (Eq. 24)



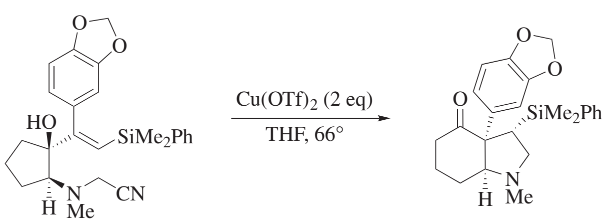
36 **37** (60%) (Eq. 25)

1,2-Disubstitution. Aza-Cope/Mannich reactions of substrates containing both internal and terminal alkene substituents give 3-acylpyrrolidines having substituents at C3 and C4. As the alkene is incorporated in a stereospecific fashion in aza-Cope-Mannich reactions, the geometry of the alkene dictates the relative configuration of these substituents. As discussed in the Stereochemistry section, substrates containing (E)-alkene fragments participate readily and with high stereoselectivity in aza-Cope/Mannich reactions (Eq. 5), whereas the stereoselection is lower in reactions of substrates containing (Z)-alkene fragments (Eq. 6).[28] High levels of stereoselectivity are reported for reactions of E-substrates containing terminal aromatic or alkyl substituents.[60] One example is depicted in Eq. 26, which also shows the compatibility of an acid-labile, *tert*-butyl ether substituent.[52]



(45%) (Eq. 26)

1,1,2-Trisubstitution. Only one account of a trisubstituted alkene taking part in an aza-Cope/Mannich reaction is on record. The viability of the silyl substituent, which is employed as an alcohol surrogate in further elaboration of the aza-Cope/Mannich product, is a notable feature of this example (Eq. 27).[46]



(94%) (Eq. 27)

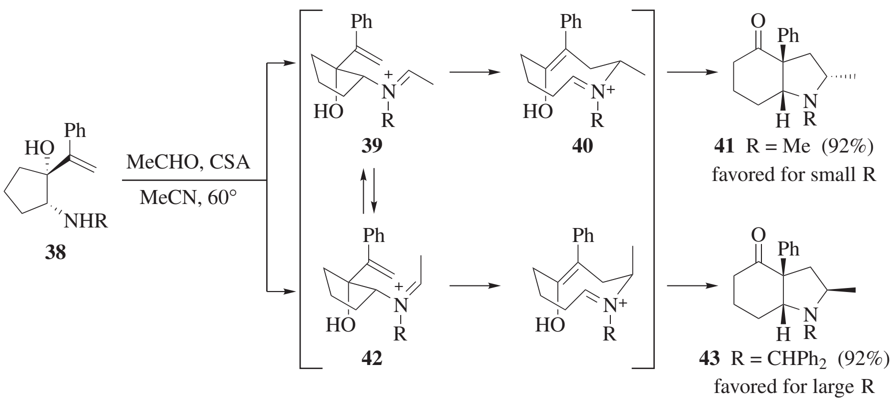
No examples of the aza-Cope/Mannich reactions with trisubstituted (*Z*)-alkenes or tetrasubstituted alkenes are known.

Nature of the Amine Substituent

As discussed earlier in the context of generating an iminium ion for the aza-Cope rearrangement, a variety of *N*-alkyl (both cyclic and acyclic) and *N*-aryl substituents are tolerated. In these reactions, either the free amine and just less than one equivalent of acid,[4] or the ammonium salt can be used.[44,45]

Two examples of the generation and use of a cyclic *N*-acyliminium ion in the aza-Cope/Mannich reaction are on record.[63,64] Both reactions proceed in <60% yield, which is lower than the typical yield realized in aza-Cope/Mannich reactions of iminium cations with reduced electrophilicity.

The stereochemical outcome of an aza-Cope/Mannich reaction can be controlled by the size of the substituent on nitrogen. This feature is exemplified in studies of ring-enlarging pyrrolidine annulation reactions of *cis*-2-amino-1-alkenylcyclopentanols **38** with acetaldehyde (Eq. 28).[66] When the nitrogen substituent is small (R = Me), the configuration-determining [3,3]-sigmatropic rearrangement (**39** → **40**) occurs preferentially via the (*E*)-iminium ion stereoisomer to give octahydroindolone **41** (R = Me) in 92% yield.[29,55] In contrast, when the amine substituent is large (R = $CHPh_2$), octahydroindolone **43** (R = $CHPh_2$) is formed in 92% yield. Destabilizing steric interactions between the vicinal methyl and benzhydryl groups in the latter case are suggested to result in preferential rearrangement of the (*Z*)-iminium ion stereoisomer by way of chair conformer **42**.



38 **39** **40** **41** R = Me (92%) favored for small R **42** **43** R = $CHPh_2$ (92%) favored for large R

(Eq. 28)

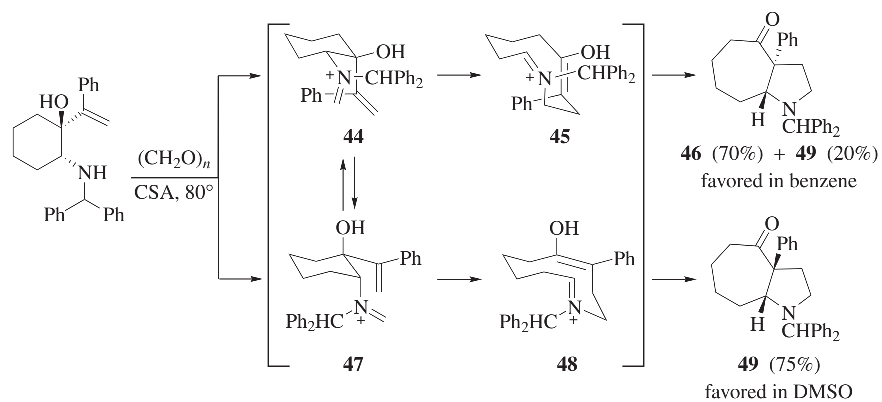
N-Substituents can serve as chiral auxiliaries to control diastereoselection in aza-Cope/Mannich rearrangements.[48,52,60,67] These examples are discussed in more detail in a later section.

Nature of the Solvent

The choice of a suitable solvent for the aza-Cope/Mannich reaction is governed largely by the method used to generate the iminium ion and the solubility of the

reactants. Reactions initiated by protic-acid-mediated carbonyl condensation or oxazolidine rupture appear to be relatively insensitive to the solvent choice, with benzene, toluene, methanol, ethanol, acetonitrile, tetrahydrofuran, nitromethane, or dimethyl sulfoxide all being used successfully. Lewis acid promoted reactions have also been carried out in a variety of solvents, including ethanol, chloroform, tetrahydrofuran, or diethyl ether.

However, the choice of solvent can affect stereoselection in aza-Cope/Mannich reactions. For example, the stereochemical outcome of the ring-enlarging pyrrolidine annulation reaction depicted in Eq. 29 is highly dependent on the choice of solvent.[50,68] In benzene, a 3.5:1 mixture of aza-Cope/Mannich products is formed in high yield favoring *trans*-cycloheptapyrrolidine **46**. In dimethyl sulfoxide, the selectivity is reversed, with *cis*-cycloheptapyrrolidine **49** being the nearly exclusive product, isolated in 75% yield. The preferential formation of *cis*-isomer **49** in dimethyl sulfoxide is ascribed to an increase in the size of the alcohol substituent in this strong hydrogen bond-accepting solvent.[50] In benzene, the two possible chair [3,3]-sigmatropic rearrangement pathways (**44** → **45** and **47** → **48**) are suggested to be balanced in energy, because destabilizing steric interactions between the ring and the phenyl or benzhydryl substituents are expected in either transition structure. In dimethyl sulfoxide, the destabilizing quasi-1,3-diaxial interaction between the hydroxy and benzhydryl substituents in the former pathway is believed to tip the balance, leading to the preferential formation of *cis*-cycloheptapyrrolidine **49**.

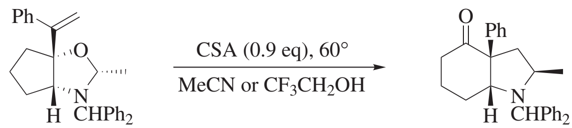


(Eq. 29)

A similar dependence on solvent is observed in a related ring-enlarging pyrrolidine annulation reaction with 2-amino-1-(1-arylethenyl)cyclopentanols, also having *cis*-oriented amine and vinyl groups.[29]

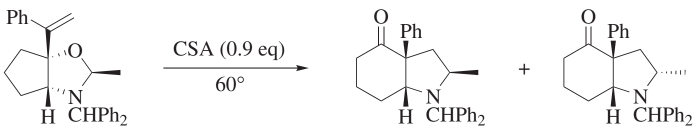
The choice of solvent can also affect stereoselectivity in reactions where equilibration of iminium ion stereoisomers occurs at a rate that is competitive with the aza-Cope/Mannich transformation. Such a scenario is suggested for ring-enlarging pyrrolidine annulations of methyloxazolidine epimers α- and β-**50** (Eqs. 30 and 31).[66] Rearrangement of the α epimer in either acetonitrile or

trifluoroethanol gives all-*cis*-octahydroindolone **51** as the exclusive product (Eq. 30). Oxazolidine epimer β-**50** also rearranges in acetonitrile with high stereoselectivity to form product **51**. However, in trifluoroethanol, methyl epimer **52** is produced preferentially from precursor β-**50**, albeit with only 2:1 selectivity (Eq. 31).[66] It is proposed that in the non-nucleophilic protic solvent trifluoroethanol, [3,3]-sigmatropic rearrangement of the (*E*)- and (*Z*)-iminium ions generated from β-**50** occurs at a rate comparable to the rate of interconversion of iminium ion stereoisomers.



(Eq. 30)

α-**50** **51** (92%) in MeCN



(Eq. 31)

β-**50** **51** **52**

MeCN, **51** + **52** (—), **51**:**52** = >100:1

CF_3CH_2OH, **51** + **52** (88%), **51**:**52** = 1:2

Nature of the Acid

Typically, the choice of protic or Lewis acid depends on the method used to initiate the aza-Cope/Mannich reaction, and/or the stability of the substrate and products to the reaction conditions, rather than any effect the acid has on the stereochemical outcome of the reaction. In initiating an aza-Cope/Mannich reaction by acid-mediated condensation between an amine and an aldehyde, typically less than one equivalent of a protic acid is used. These effectively neutral reaction conditions tolerate a number of potentially acid-sensitive functional groups, such as tertiary allylic alcohols, as shown in many of the examples in this review, primary amines,[65] triisopropylsilyl ethers,[45] *tert*-butyl ethers,[32,33] *tert*-butyl esters,[37] and *tert*-butyl carbamates.[35,38] The compatibility of these groups is a testament to the mild conditions generally used for the aza-Cope/Mannich reactions.

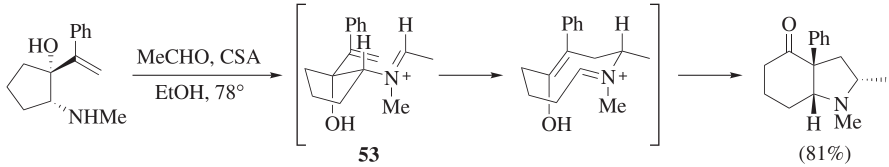
Although substoichiometric amounts of a protic acid are typically used for condensation of 1-aminobut-3-en-2-ol-containing substrates with non-bulky aldehydes, if reaction with a ketone is desired, then conversion into an oxazolidine is often necessary. Typically, generation of the iminium ion from the oxazolidine is unsuccessful with catalytic amounts of a protic acid, with one equivalent needed to promote the reaction.[31,59]

Stoichiometric amounts of Lewis acids such as diethylaluminum chloride[43] or the boron trifluoride–diethyl ether complex can be used to generate an iminium ion from an oxazolidine precursor.[60] These reagents allow the use of cryogenic temperatures, which can be desirable in maintaining sensitive functional groups such as acetals.[42,60]

Diastereoselectivity

As introduced in the Stereochemistry section, one of the most important attributes of the aza-Cope/Mannich reaction is its high and predictable stereoselectivity. There are three major factors that determine the stereochemical outcome: (1) the bias for the aza-Cope rearrangement to proceed by a chair geometry, which for a substrate containing an (E)-alkene can be >3 kcal/mol;[28] (2) the preferential rearrangement of iminium ion stereoisomers that place substituents in quasi-equatorial positions in favored chair transition structures; and (3) the facility of intramolecular Mannich cyclizations, which generally occur faster than loss of configurational homogeneity of the enol or iminium ion π-bonds generated in the aza-Cope rearrangement.

Many of the diastereoselective aza-Cope/Mannich reactions described to date are of cyclic substrates and result in ring-enlarging pyrrolidine annulations. When the vinyl and amine units of such substrates are *trans*, and the starting ring is not large, only two transition structures—the favored chair and usually disfavored boat—bring the vinyl and iminium ion termini within bonding distance. The chair rearrangement geometry leads to clean formation of the *cis*-fused product (Eqs. 19, 20, Scheme 2, Eqs. 22–25, 28, 30–32).[25,29,36–38,46,47,50,55,65,66] When the iminium ion is derived from an aldehyde other than formaldehyde, the substituent adjacent to nitrogen typically emerges on the more hindered concave face of the *cis*-bicyclic unit. This outcome arises from preferential rearrangement of the (E)-iminium ion stereoisomer **53**, which places the substituent in a favored pseudo-equatorial position (Eq. 32).[29,55] That these reactions are kinetically and not thermodynamically controlled is apparent. As discussed previously, preferential rearrangement of the (Z)-iminium ion can be obtained if the nitrogen substituent is very large, in which case the substituent on the formyl group emerges on the convex face (Eq. 28).

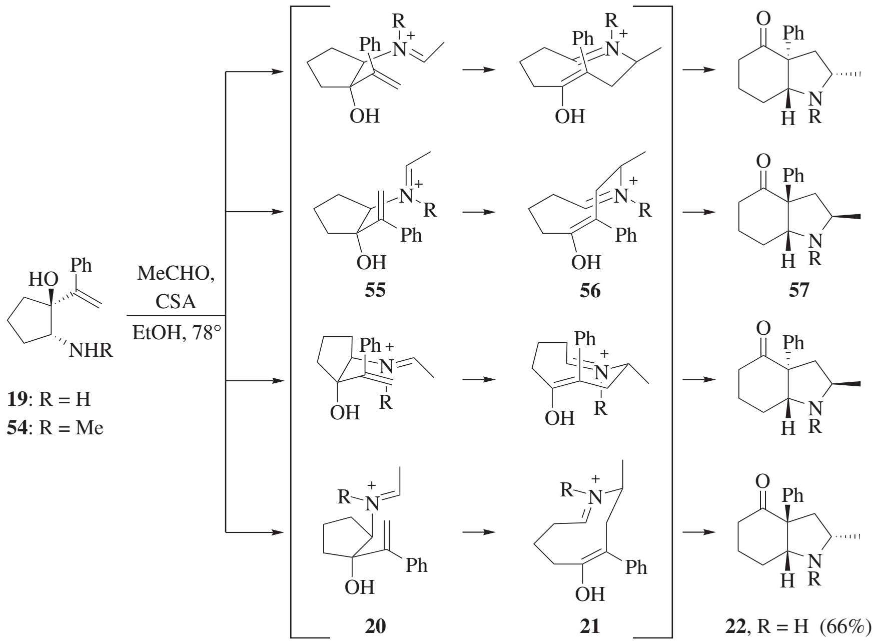


53

(Eq. 32)

The situation is more complex when the amine and vinyl units are *cis*. In these cases, four rearrangement geometries must be considered: two chair and two boat (Eq. 33). Assuming that the Mannich reaction of the presumed azacyclononadiene intermediate is more rapid than any loss of stereochemical integrity of this species, two geometrically different pathways can lead to the *cis*-octahydroindolone product: **20** → **21** and **55** → **56**. In the aza-Cope/Mannich rearrangement of primary amine precursor **19**, the observed formation of *cis*-octahydroindolone **22** (R = H) with an α-oriented methyl group is consistent with preferential [3,3]-sigmatropic rearrangement of the (E)-iminium ion by a chair geometry to generate (E,Z)-azacyclononadiene intermediate **21** instead of the presumably

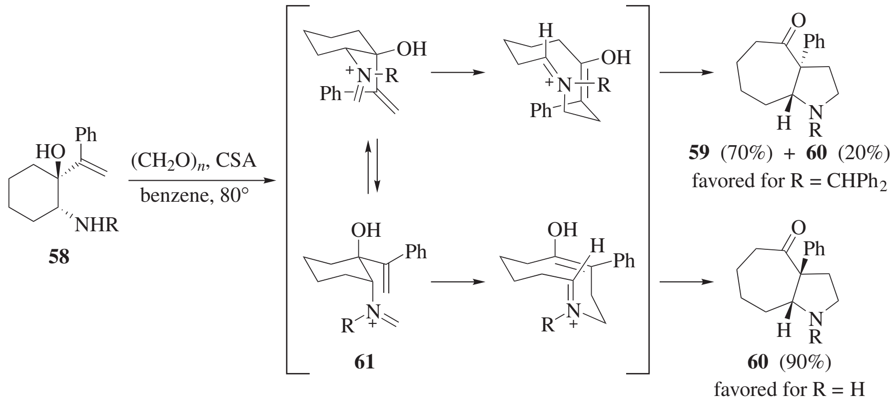
more stable (Z,Z)-azacyclononadiene intermediate **56**.[69] As noted earlier, this transformation is one of several instances where aza-Cope rearrangements appear to differ substantially from cognate rearrangements of hydrocarbons.[30] The additional complexity in predicting stereoselection in this series is highlighted in the aza-Cope/Mannich reaction of N-methyl congener **54** and acetaldehyde. In this case, a mixture of *cis*-hydroindolones **22** (R = Me) and **57** (R = Me) is formed in all solvents investigated.[29] That the **20** → **21** pathway would be less favored in this series is not surprising, because the N-methyl substituent would be thrust over the cyclopentane ring.



(Eq. 33)

As discussed previously, the size of the amine substituent can also affect stereoselection in aza-Cope/Mannich reactions (Eq. 28). An additional example is summarized in Eq. 34.[50,68] When the amine substituent is small (R = H), ring-enlarging pyrrolidine annulation of precursor **58** gives exclusively *cis*-hydrocyclohepta[*b*]pyrrole **60** in 90% yield. In this case, rearrangement via chair geometry **61** is proposed to be highly favored to avoid placing the bulky phenyl substituent under the cyclohexane ring. When the amine substituent is large (**58**, R = benzhydryl), a 3.5:1 mixture of products favoring *trans*-hydrocyclohepta[*b*]pyrrole **59** is formed in 90% yield. The two chair rearrangement transition structures are more similar in energy in the latter case, as

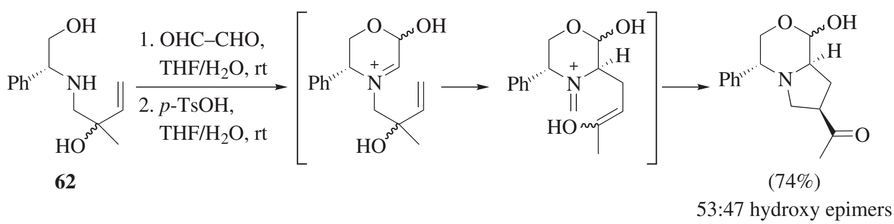
destabilizing steric interactions with the phenyl or benzhydryl group are expected in either chair transition structure.



(Eq. 34)

Enantioselectivity

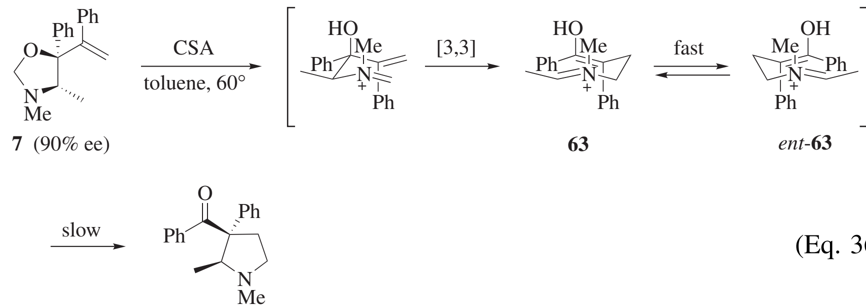
Diastereoselectivity Resulting from a Chiral Auxiliary. As will be discussed below, the aza-Cope/Mannich reaction is not well suited to access simple chiral non-racemic pyrrolidines in high enantiomeric purity. A simple method to overcome this limitation is to use a removable chiral auxiliary. An example is the synthesis of precursor **62** from (*R*)-phenylglycinol and use of the benzylic stereocenter to control facial selection in the sigmatropic rearrangement step (Eq. 35).[24,52,67,70]



(Eq. 35)

Asymmetric Induction without a Chiral Auxiliary. Aza-Cope/Mannich rearrangements of chiral, enantioenriched 1-aminobut-3-en-2-ol precursors lead to racemic 3-acylpyrrolidine products when the aza-Cope rearrangement step produces an intermediate lacking stereogenic centers (Eq. 3).[25] Although the product of a chair geometry, [3,3]-sigmatropic rearrangement in this example, iminium ion/enol **63**, would be formed initially in a chiral conformation, it can racemize to *ent*-**63** by simple single-bond rotations (Eq. 36). Because this conformational

interconversion is faster than intramolecular Mannich cyclization, racemic 3-acylpyrrolidine **8** is generated.

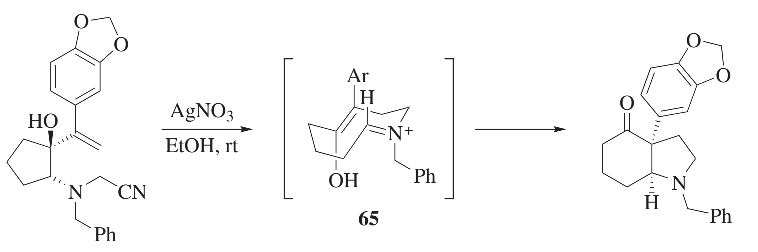


7 (90% ee) **63** *ent*-**63**

8 (79%) racemic

(Eq. 36)

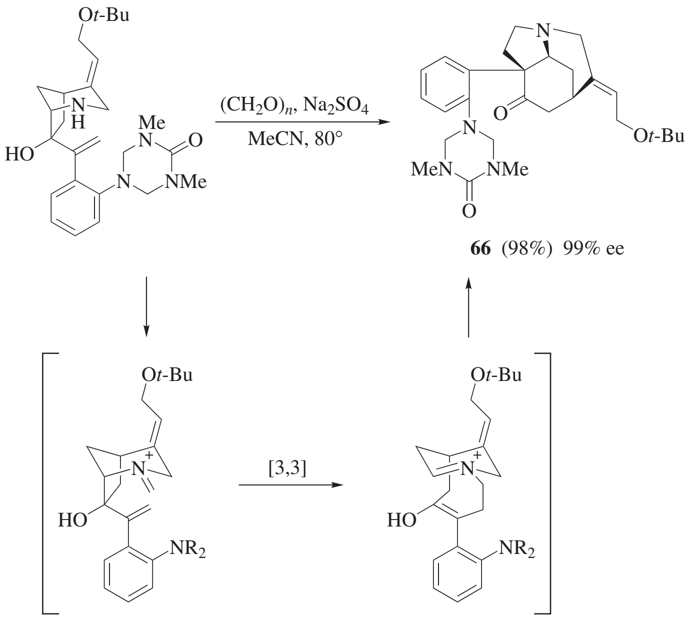
However, the limitation described above does not extend to ring-enlarging variants of the aza-Cope/Mannich reaction. The conversion of enantiomerically pure 1-alkenyl-2-aminocyclopentanol **64** to the enantiomerically pure *cis*-hydroindolone illustrates this point (Eq. 37).[25] In this case, racemization of the likely intermediate in this sequence, azacyclononadiene **65**, is retarded by the conformational constraints of the medium-sized ring.



64 enantiomerically pure **65** (−) enantiomerically pure

(Eq. 37)

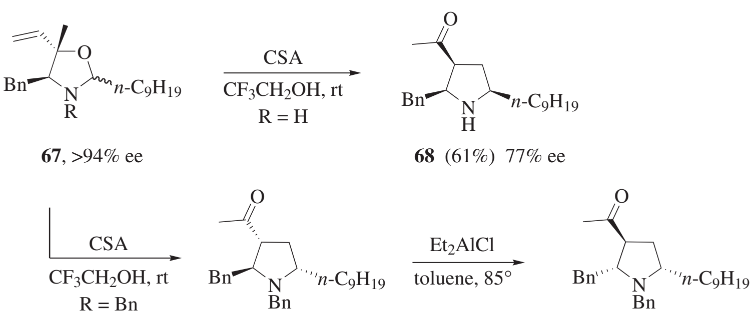
In many applications of the aza-Cope/Mannich reaction to the synthesis of polycyclic ring systems, the product of the aza-Cope rearrangement contains a stereogenic center that cannot readily epimerize. In such cases, no loss of enantiomeric purity is possible in the cascade transformation. One example is the aza-Cope/Mannich rearrangement step in the synthesis of (−)-strychnine, where pentacyclic product **66** is formed in nearly quantitative yield with no loss of enantiomeric purity (Eq. 38).[32,33]



66 (98%) 99% ee

(Eq. 38)

If a stereogenic center is generated in the aza-Cope rearrangement step, asymmetric induction should be possible in the formation of simple 3-acylpyrrolidines by the aza-Cope/Mannich reaction. This possibility was examined in detail during the synthesis of the antifungal antibiotic preussin.[43] Acid-promoted rearrangement of oxazolidine **67**, in which the nitrogen is unsubstituted (R = H), generates the enantiomerically enriched (2*S*,3*S*,5*R*)-acetylpyrrolidine **68** in 61% yield; however, ca. 20% erosion of enantiomeric purity is observed (Scheme 3). In contrast, *N*-benzyloxazolidine **67** rearranges under identical conditions with a smaller loss of enantiomeric purity (87% ee) to give (2*S*,3*R*,5*S*)-acetylpyrrolidine **69**, which has a *trans* relationship between the C2 benzyl and C5 nonyl groups. On treatment with diethylaluminum chloride at 85°, the latter product is converted into the



67, >94% ee

68 (61%) 77% ee

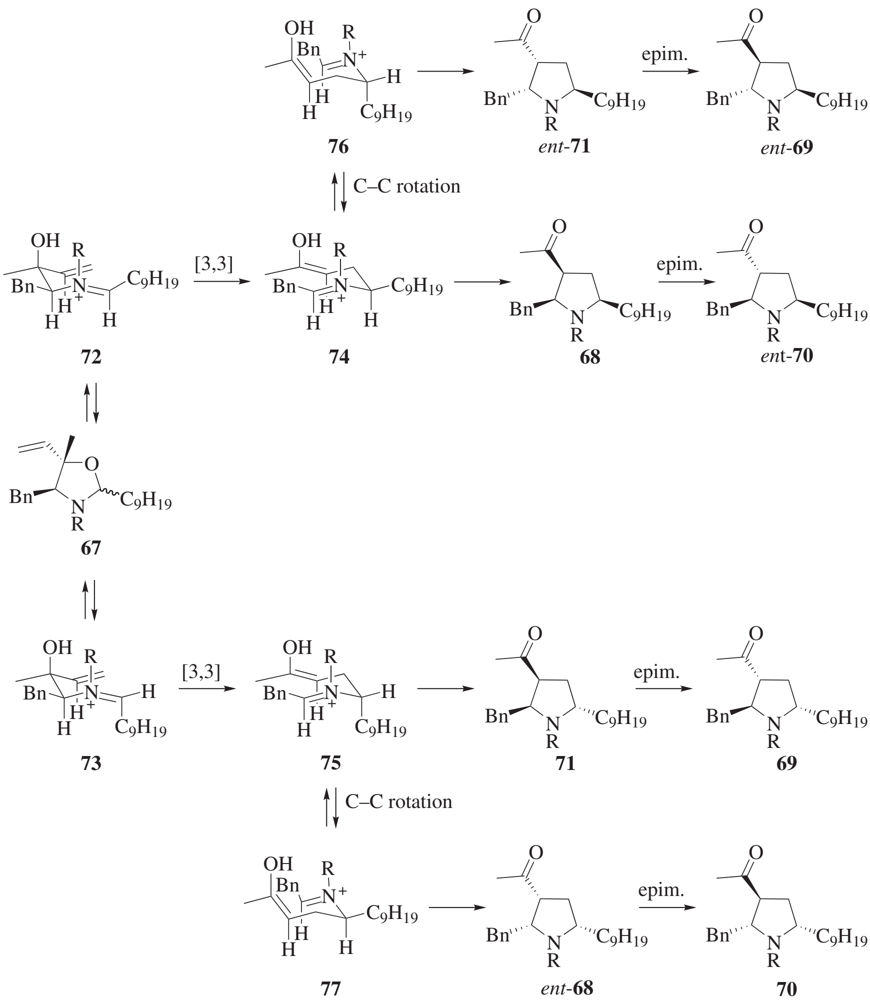
69, 87% ee

70 (61%) over 2 steps, 87% ee

Scheme 3

thermodynamically favored diastereomer **70** without loss of enantiomeric purity, presumably by a retro-Mannich/Mannich sequence.

To rationalize how the change in reaction outcome depends on the amine substituent and why the partial erosion of enantiopurity is observed, several assumptions are made, most of which have been discussed previously: (1) the [3,3]-sigmatropic rearrangement occurs by a chair geometry; (2) intramolecular Mannich cyclization is more rapid than stereomutation of the enol and iminium groups; and (3) pyrrolidines bearing a *cis*-relationship of the acetyl and benzyl groups can epimerize at C3. As depicted in Scheme 4, even with these assumptions, all eight possible stereoisomeric acetylpyrrolidine products (four



Scheme 4

enantiomer pairs) can be formed.[43] The analysis in the N-unsubstituted series is fairly straightforward. The (E)-iminium stereoisomer generated by acid-mediated ring opening of oxazolidine **67** (R = H) should be more stable than its Z-stereoisomer. This intermediate should preferentially undergo aza-Cope rearrangement via isomer **72** (R = H) in which the benzyl group occupies a quasi-equatorial orientation to generate constitutional isomer **74** (R = H). Intramolecular Mannich cyclization of this intermediate from the *re* face of the iminium ion would give the ($2S,3S,5R$)-acetylpyrrolidine **68** (R = H), as is observed. Mannich cyclization from the alternative *si* face would be disfavored because the n-nonyl substituent would experience a destabilizing $A^{1,3}$-interaction (e.g., cyclization via conformer **76**). The observed partial racemization is interpreted to mean that the (Z)-iminium ion produced from ring opening of oxazolidine **67** (R = H) to some extent undergoes aza-Cope rearrangement via conformer **73** (R = H) to generate isomer **75** (R = H), which preferentially cyclizes from the *si* face of the iminium ion (i.e., via isomer **77**) to ultimately generate the ($2R$,$3R$,$5S$)-acetylpyrrolidine *ent*-**68** (R = H).

This study highlights the ease with which enantiomeric purity can be eroded during an aza-Cope/Mannich reaction to access 2,5-disubstituted 3-acylpyrrolidines. All that is required is for the aza-Cope rearrangement to take place from the alternate iminium ion stereoisomer, which ‘epimerizes’ C5, and the Mannich cyclization to occur from the alternate stereoface of the rearranged iminium cation, which ‘epimerizes’ C2 and C3.

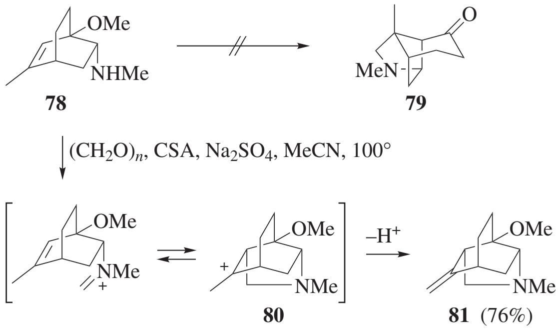
The preferential formation of ($2S$,$3R$,$5S$)-acetylpyrrolidine **69** (R = Bn) from oxazolidine **67** where R = Bn is less straightforward to explain. A speculative rationale in which the (Z)-iminium stereoisomer is preferentially generated by acid-mediated ring opening of oxazolidine **67** (R = Bn) and reacts by a **73** → **75** → **71** → **69** (R = Bn) pathway has been advanced.[43]

Examples of asymmetric induction in the aza-Cope/Mannich reaction of an achiral starting material making use of an external chiral reagent are unknown.

Limitations

Besides the limitations noted in our previous discussion of various aspects of the aza-Cope/Mannich reaction, failure to realize this conversion with a bridged-bicyclic substrate merits note. During early investigations toward the total synthesis of the alkaloid gelsemine, an aza-Cope/Mannich reaction of bicyclo[2.2.2]octene **78** was examined as a potentially straightforward route to assemble the azatricyclo[4.4.0.0^{2,8}]decane core **79** of this alkaloid (Eq. 39).[53,71] However, condensation of amine **78** with paraformaldehyde results in aza-Prins cyclization to form azatricyclodecane **81**. Replacing the methyl substituent on the double bond with an electron-withdrawing ester substituent, with the aim of destabilizing the carbenium ion intermediate analogous to **80**, also fails to promote an aza-Cope/Mannich transformation. The failure in this system to realize an aza-Cope rearrangement likely arises from the additional ring strain involved in the transition structure for the [3,3]-sigmatropic rearrangement in which the iminium carbon bonds to the distal end of the bicyclo[2.2.2]octene double bond. Although this problem is circumvented by the use of a two-step,

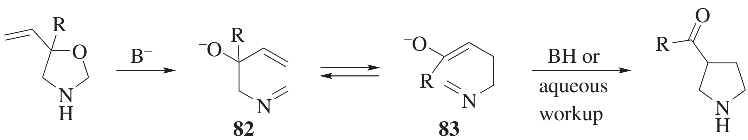
base-mediated anionic aza-Cope rearrangement–Mannich cyclization sequence, this solution falls outside the scope of this review.[53,72]



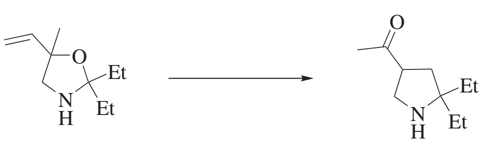
(Eq. 39)

Base-Promoted Aza-Cope/Mannich Reaction

Thus far this review has focused on the cationic variant of the aza-Cope/Mannich reaction (Eq. 1). Although much less developed, a related transformation of *N*-unsubstituted 5-vinyloxazolidines to 3-acylpyrrolidines is brought about by reaction with a base (Eq. 40).[61,62] Whereas a cationic aza-Cope rearrangement takes advantage of the rate enhancement offered by a positively charged nitrogen, the sigmatropic rearrangement step in the base-promoted reaction, (i.e., **82** → **83)** is accelerated by the presence of the allylic alkoxide substituent.[73] This variation has received scant attention since the initial report, even though some distinct advantages are offered. Under the conditions initially reported, the cationic aza-Cope/Mannich reaction is only successful with oxazolidines derived from non-bulky aldehydes or cyclohexanone derivatives.[31,59] The base-promoted aza-Cope/Mannich reaction overcomes these limitations, with a variety of oxazolidines derived from ketones and aldehydes being successfully used in the reaction (Eq. 41).[61] Typically an excess of potassium hydride, tritylpotassium, or potassium hydroxide is used, often in combination with catalytic amounts of 18-crown-6. Sodium hydride or *n*-butyllithium are unsuccessful, which is in accord with the lower activation provided by sodium or lithium alkoxides in the base-accelerated oxy-Cope rearrangement.[73,74]



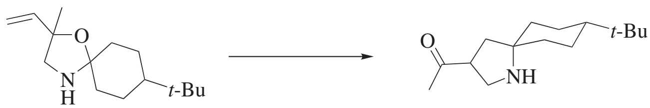
(Eq. 40)



(Eq. 41)

CSA (1 eq), benzene, 80° (9%)
KH (1.5 eq), 18-crown-6, THF, rt (82%)

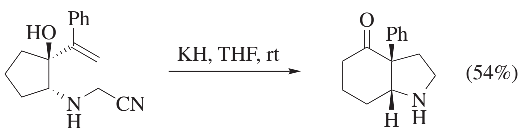
Although little examined at this point, stereoselection appears to be lower in the base-promoted process. Such is the case in the formation of 1-azaspiro[5.4]decane **85** from oxazolidine **84** (Eq. 42). Whereas cationic conditions give a 92:8 mixture of stereoisomers, with isomer **85** predominating,[31] the basic conditions result in a 3:2 mixture of products favoring the same epimer.[61] Compared to the preference for equatorial carbon–carbon bond formation in analogous Claisen rearrangements, the cationic aza-Cope/Mannich reaction shows a higher preference, whereas it appears to be similar for the base-mediated process.[75]



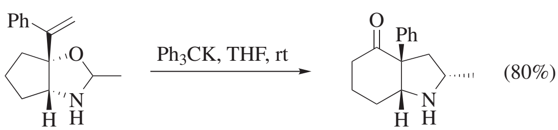
84 **85** (Eq. 42)

CSA (1 eq), benzene, 80° (70%) 92:8 dr
KH (1.5 eq), 18-crown-6, THF, rt (91%) 60:40 dr

The ring-enlarging pyrrolidine annulation variation of the aza-Cope/Mannich reaction is also successful under basic conditions, with cyanomethyl-substituted amines and oxazolidines being used as precursors (Eqs. 43 and 44).[62] However, the yields of these transformations are typically diminished compared to those realized under acidic conditions.



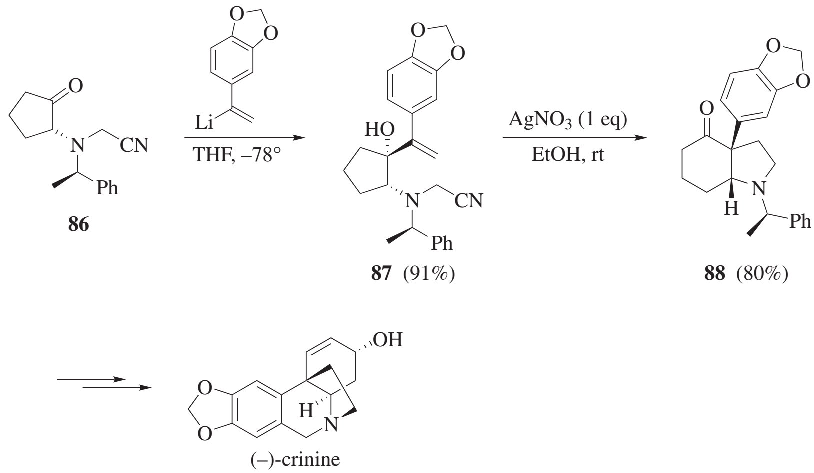
(Eq. 43)



(Eq. 44)

APPLICATIONS TO SYNTHESIS

Because of its high levels of predictable stereocontrol and its compatibility with most functional groups, the aza-Cope/Mannich reaction has found significant application in target-directed natural product synthesis. An early example is the asymmetric, total synthesis of the *Amaryllidaceae* alkaloid (−)-crinine, which is accomplished in 10 steps and 6% overall yield using the ring-enlarging pyrrolidine annulation variant of the aza-Cope/Mannich reaction as the pivotal step (Scheme 5).[48] An (*R*)-α-methylbenzylamine chiral auxiliary is used to assemble cyclopentanone **86** in high enantiomeric purity. Vinyllithium addition to this α-amino ketone occurs with high diastereoselectivity to give precursor **87**. The latent iminium ion within **87** is then unmasked by reaction with one equivalent

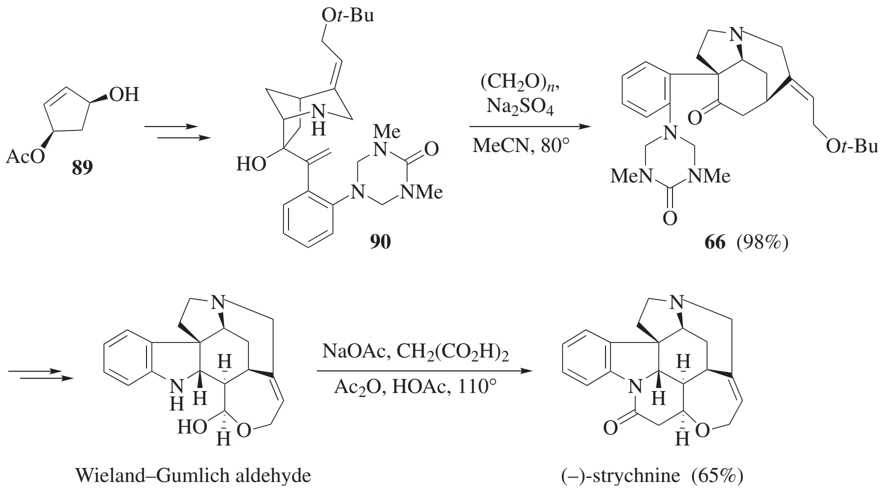


Scheme 5

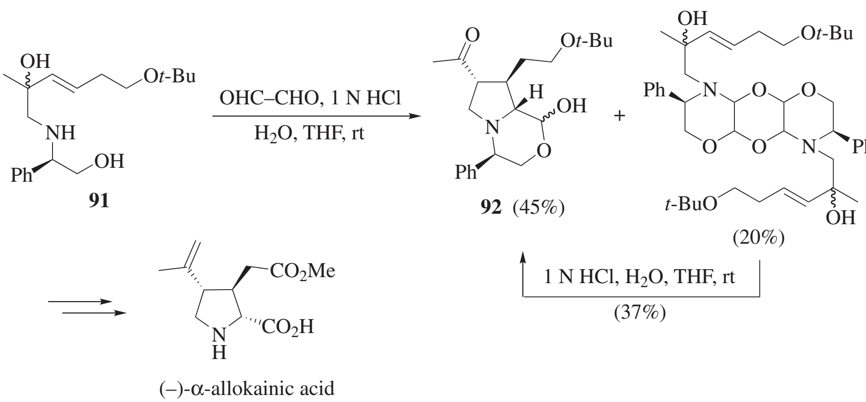
of silver nitrate, which initiates the aza-Cope/Mannich reaction to give perhydroindolone **88** in 80% yield as a single stereoisomer. In six conventional steps, this product is converted into (−)-crinine.

The success of the aza-Cope/Mannich reaction for the synthesis of (−)-crinine was followed by the synthesis of more than a dozen alkaloids using this transformation.[32,33,35–38,41,44–48,60,65] Several key steps in the first asymmetric synthesis of (−)-strychnine are summarized in Scheme 6.[32,33] The synthesis begins with enantiopure allylic alcohol **89**, which is available on a large scale by enzymatic desymmetrization of the *meso*-diacetate precursor. In fourteen steps, intermediate **90** is accessed. The crucial aza-Cope/Mannich transformation is accomplished in essentially quantitative yield on a multigram scale on heating amino alcohol **90** in acetonitrile with excess paraformaldehyde and anhydrous sodium sulfate to give pentacyclic product **66** containing the critical D, E, and F rings and *Z* double bond of strychnine. In five further steps, the Wieland–Gumlich aldehyde is accessed, which on reaction with malonic acid and acetic anhydride gives (−)-strychnine in 65% yield. This sequence was also used to prepare *ent*-strychnine, starting from the enantiomer of **89**.[76]

An example of the use of the aza-Cope/Mannich reaction for synthesis of a simple pyrrolidine natural product is provided in the total synthesis of (−)-α-allokainic acid (Scheme 7).[52] In this enantioselective synthesis, (*R*)-phenylglycinol is used as a chiral auxiliary to control the diastereoselectivity of the aza-Cope/Mannich reaction. Reaction of enantiomerically pure amino alcohol **91** with two equivalents of glyoxal in slightly acidic aqueous medium (pH 4–5) gives in moderate yield pyrrolidine **92**, in which three contiguous stereocenters are generated. A tricyclic compound is also isolated as a result of condensation of two equivalents of amino alcohol **91** with glyoxal. Resubjection of this product



Scheme 6

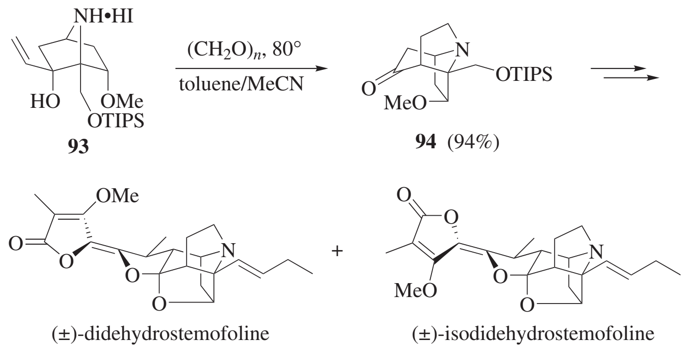


Scheme 7

to the same acidic medium gives pyrrolidine **92** in 37% yield. In ten further steps, this product is transformed into (−)-α-allokainic acid.

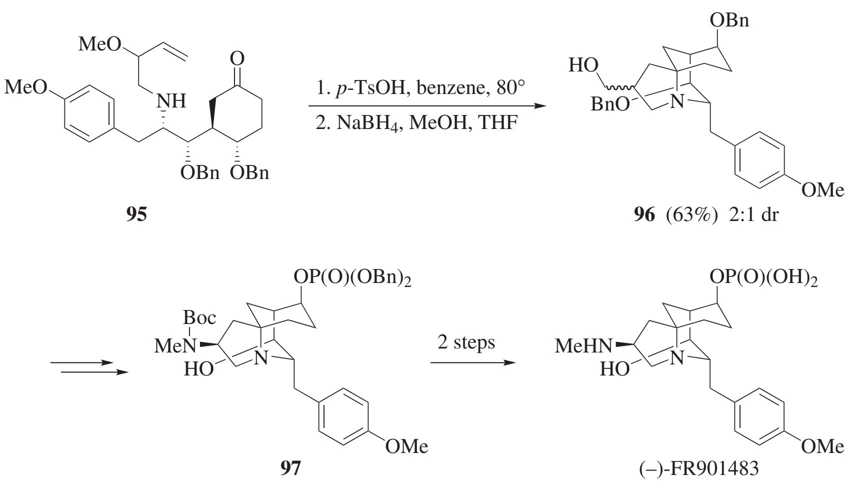
An example of the use of the aza-Cope/Mannich reaction to assemble a bridged-tricyclic structure is provided in the first total syntheses of the intricate *Stemona* alkaloids (±)-didehydrostemofoline and (±)-isodidehydrostemofoline (Scheme 8).[45] The central 1-azatricyclo[5.3.0.0^{4,10}]decanone moiety of these alkaloids is constructed in nearly quantitative yield on heating 1-azabicyclo[2.2.1]heptane salt **93** with an excess of paraformaldehyde at 80°. Product **94** is then elaborated in 16 steps to (±)-didehydrostemofoline and (±)-isodidehydrostemofoline. This aza-Cope/Mannich reaction illustrates that perfect

overlap is not required for a successful aza-Cope rearrangement, as the rigidity of the 1-azabicyclo[2.2.1]heptane precludes ideal overlap of the termini of the formaldiminium ion and vinyl substituent.



Scheme 8

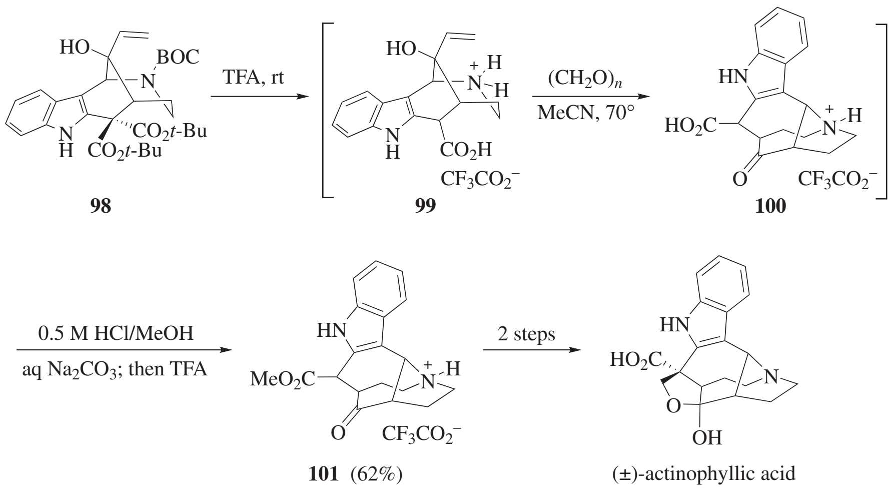
A formal asymmetric synthesis of the immunosuppressant (−)-FR901483 was accomplished by using a cationic aza-Cope/Mannich approach (Scheme 9).[40] This synthesis was the first of this natural product to control the configuration of both oxygen-bearing stereocenters. In the key step, intramolecular condensation of keto amine **95** on reaction with *p*-toluenesulfonic acid in refluxing benzene generates a bridgehead iminium ion, which initiates an aza-Cope/Mannich reaction to give a tricyclic product as a mixture of aldehyde epimers. This product is unstable to silica gel chromatography, so a direct reduction with sodium borohydride is carried out to provide azatricyclododecane **96** as a mixture of hydroxymethyl isomers



Scheme 9

favoring the α epimer. The minor isomer is advanced to tricyclic intermediate **97** in seven steps, thus completing a formal total synthesis of (−)-FR901483.

The aza-Cope/Mannich reaction is of particular value in synthesis when it is used to rapidly generate structural complexity from a simple, readily available precursor. A good illustration is provided in the recent total synthesis of (±)-actinophyllic acid (Scheme 10).[44] In five steps from di-*tert*-butyl malonate, tetracyclic allylic alcohol **98** is prepared as a single diastereomer. In a notable one-pot process, this intermediate is converted into pentacyclic ester **101** in 62% yield. Addition of trifluoroacetic acid at room temperature results in cleavage of the Boc and *tert*-butyl groups of **98**, giving after decarboxylation amino acid **99**. Removal of the excess trifluoroacetic acid under vacuum, dilution with acetonitrile, and exposure to paraformaldehyde at 70° promotes the aza-Cope/Mannich reaction to yield pentacyclic acid **100**. Fischer esterification then provides amino ester salt **101** in 62% yield as an inconsequential 1:1 mixture of ester epimers. In two further steps, the first total synthesis of (±)-actinophyllic acid is completed.



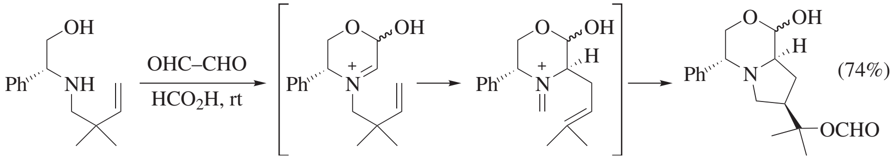
Scheme 10

COMPARISON WITH OTHER METHODS

The plethora of pyrrolidine syntheses in the literature is testimony to the importance of this ring system. Few of these methods match the breadth, regiocontrol, stereocontrol, and mildness of the aza-Cope/Mannich reaction. To give a suitable comparison to the aza-Cope/Mannich reaction, this discussion will focus on those methods that construct the pyrrolidine from acyclic precursors by forming two bonds in a single reaction.

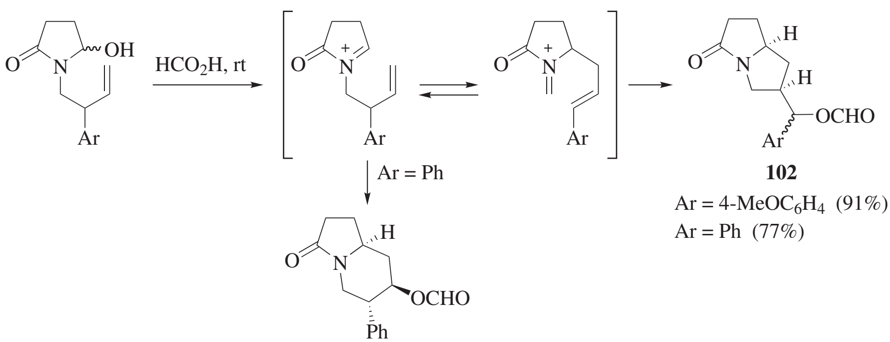
The pyrrolidine construction that is mechanistically most related to the aza-Cope/Mannich reaction is a cascade sequence in which an aza-Prins cyclization

follows an aza-Cope rearrangement.[70] One example leading to an enantiomerically enriched product from the studies of Couty and co-workers is illustrated in Eq. 45.[77]



(Eq. 45)

Several reports of related sequences are known in which [3,3]-sigmatropic rearrangement of an unsaturated *N*-acyliminium ion precedes an aza-Prins cyclization.[78,79] Two examples are illustrated in Eq. 46.[22] When the aryl group is *p*-methoxyphenyl, pyrrolizidinone **102** (Ar = 4-$MeOC_6H_4$) is formed in 91% yield as the exclusive product. When the alkene generated on aza-Cope rearrangement is a less-nucleophilic styrene, the aza-Cope rearrangement is believed to be reversible, in which case pyrrolizidinone **102** (Ar = Ph) is obtained in 77% yield with indolizidinone **103** also being formed. This example illustrates one difference between the aza-Cope/Mannich reaction and the related aza-Prins-terminated sequence in that the enol nucleophile generated in the sigmatropic rearrangement of the former cascade process is more reactive, resulting in most cases in efficient trapping of the product iminium ion.



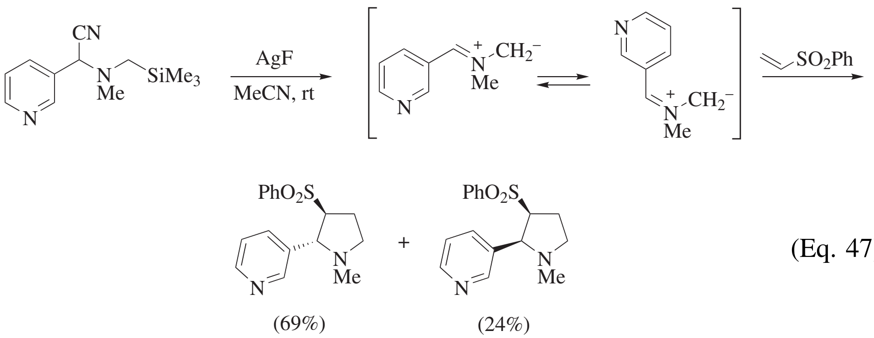
102
Ar = 4-$MeOC_6H_4$ (91%)
Ar = Ph (77%)

103 (7%)

(Eq. 46)

1,3-Dipolar cycloaddition of azomethine ylides with dipolarophiles is a widely utilized reaction that provides reliable access to substituted pyrrolidines by the formation of two carbon–carbon bonds.[80] The method requires an electron-deficient alkene. A number of methods are available for azomethine ylide generation, with one of the more popular being fluoride-mediated desilylation of cyanoaminosilanes (Eq. 47).[81] Many other methods have been used to generate the azomethine ylides for intermolecular 1,3-dipolar cycloaddition, including

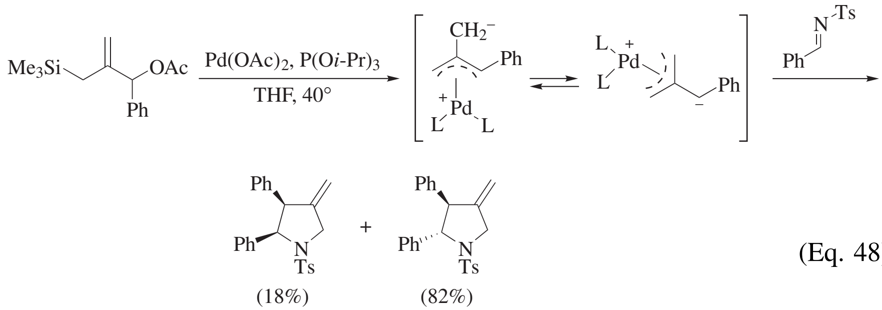
oxazoline fragmentation,[82–84] deprotonation of tertiary *N*-oxides,[85] rhodium-mediated dipole cascades,[86,87] thermal 1,2-prototropic shifts,[88] and decarboxylation.[89] Ring fragmentation of 2-carboxy aziridines is also used to generate azomethine ylides, although the cycloaddition is not observed in an intermolecular fashion with monoactivated alkenes.[90] Intramolecular cycloaddition in this case has been far more successful, with notable examples featured in two approaches toward the core of the complex marine alkaloid sarain A.[91,92] The limitation of this fragmentation method for azomethine ylide generation is the need for flash vacuum thermolysis at elevated temperatures (typically 300–400° at 0.04 mm Hg), which can preclude the use of sensitive functionality in the substrate.



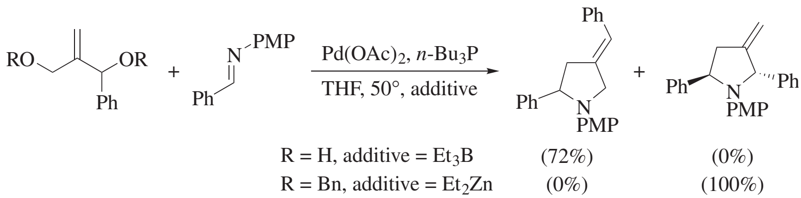
(Eq. 47)

Azomethine ylide cycloaddition, like the aza-Cope/Mannich reaction, can be used to generate enantioenriched pyrrolidines.[93] The vast majority of examples utilize either chiral auxiliaries or internal diastereoselection as methods to ensure high levels of enantiopurity. In contrast to the aza-Cope/Mannich reaction, catalytic enantioselective methods are known. Currently, this method is limited to the use of aryl azomethine ylides which results in the formation of pyrrolidines with 2-aryl substitution; isopropyl or cyclohexyl substitution leads to only moderate asymmetric induction.[94]

An alternative 1,3-dipolar cycloaddition reaction that provides access to substituted pyrrolidines by formation of one carbon–carbon and one carbon–nitrogen bond is the reaction of a trimethylenemethane palladium complex with an imine (Eq. 48).[95] Because of the nature of the dipole, the reaction is typically limited to accessing pyrrolidines with alkylidene groups in the C4 position. The trimethylenemethane palladium complex is usually generated by treatment of a trimethylsilyl propenyl acetate with a catalytic amount of low-valent palladium. *N*-Tosyl imines derived from aliphatic and aromatic aldehydes and ketones are good substrates for this process, although lower yields are typically observed if the imine can isomerize to the enamine.[96,97] With substituted trimethylenemethane sources, potential issues of regiocontrol arise, though with the correct choice of reaction parameters and starting materials, controlled access to different regioisomers is possible (Eq. 49).[97,98]



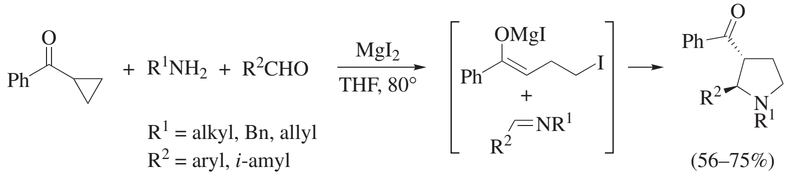
(Eq. 48)



(Eq. 49)

The [3 + 2] cycloaddition of trimethylenemethane with activated imines can be performed in a catalytic asymmetric fashion.[99] Although excellent levels of asymmetric induction are possible, the reaction is currently limited to *N*-aryl or *N*-Boc imines derived from aromatic aldehydes. *N*-Aryl imines derived from aliphatic aldehydes lead to mixtures of products.

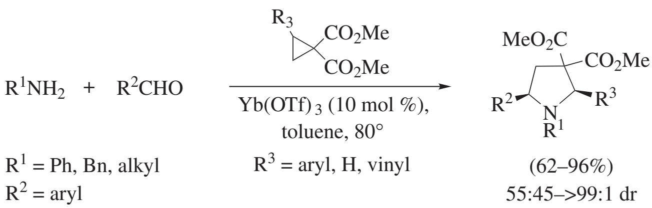
Ring opening of cyclopropyl ketones with metal iodides generates useful ambiphilic intermediates bearing both a nucleophile and an electrophile. Reaction of these species with in situ-generated imines allows access to functionalized 3-acylpyrrolidines. Although the reaction was initially developed for access to spiro[oxindole-3,3′-pyrrolidines] from 3-spirocyclopropyl-2-oxindoles,[100] later examples expanded the scope of this reaction to include methylenecyclopropyl amides.[101] In analogy to the aza-Cope/Mannich reaction, stereocontrolled access to simple *trans*-2,3-disubstituted-3-acylpyrrolidines is also possible by this method (Eq. 50).[102] In contrast to the aza-Cope/Mannich reaction, this reaction is limited to the use of aryl or branched aliphatic aldehydes, with linear aliphatic aldehydes giving little to no product.



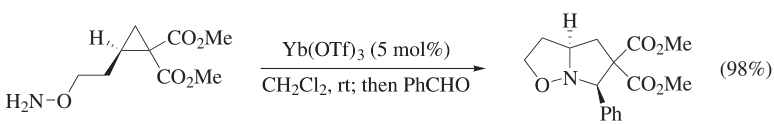
(Eq. 50)

A related reaction involving the addition of imines derived from aromatic aldehydes to activated cyclopropane diesters in the presence of catalytic amounts

of ytterbium triflate gives substituted 2,5-*cis*-disubstituted pyrrolidines. Good to excellent yields are obtained with usually good levels of diastereoselectivity (Eq. 51).[103] This reaction was successfully applied in a slightly modified form in an asymmetric total synthesis of (−)-FR901483.[104] The required use of aromatic aldehydes, and the unavoidable diester substitution at the C4 position of the pyrrolidine product, limit the widespread utility of the method. This method has also been extended to the intramolecular reaction of oxime ethers and cyclopropane diesters to give substituted bicyclic pyrrolidines.[105] Use of a hydroxylamine starting material gives 2,5-*cis*-disubstituted pyrrolidines (Eq. 52), whereas first generating the (E)-oxime allows access to 2,5-*trans*-disubstituted pyrrolidines. Like the aza-Cope/Mannich reaction, this methodology has been applied to complex alkaloid syntheses, with a recent synthesis of (−)-allosecurinine completed using this reaction as the crucial step.[106]



(Eq. 51)



(Eq. 52)

EXPERIMENTAL CONDITIONS

An attractive feature of the aza-Cope/Mannich reaction is its experimental simplicity. In many cases the reaction can be carried out by simply adding an aldehyde and less than one equivalent of a protic acid to a substrate containing the 1-amino-3-buten-2-ol fragment in a solvent, followed by heating at 50−82°. The reaction appears insensitive to the order of addition of reagents, with little conversion seen until heating is begun.

Camphorsulfonic acid (typically 0.9 equivalent) has been used most commonly; however, most strong acids should work. Catalytic amounts (0.1 equivalent) of protic acids have also been employed, though examples are less common. Although an anhydrous solvent is often used, sometimes in the presence of sodium sulfate to promote a dehydrative condensation, the exclusion of water is not always necessary, with some reactions being carried out in tetrahydrofuran/water mixtures. The reaction is generally insensitive to the choice of solvents, with benzene, toluene, or acetonitrile most commonly used. The reaction is often run under an inert atmosphere, but there appears to be little requirement for this.

Generation of an iminium ion from a cyanomethyl precursor is typically accomplished by adding solid silver nitrate to a solution of a cyanomethylamine

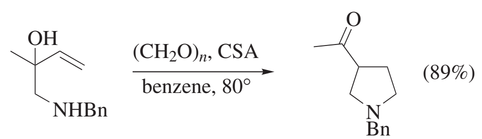
in ethanol, followed by heating to 50°. Appropriate care must be taken when using silver nitrate as it is toxic and corrosive, and extended exposure can lead to argyria. Other cyanide scavengers, such as silver acetate, silver trifluoroacetate, copper trifluoroacetate, or copper triflate have also been used.

Stoichiometric amounts of Lewis acids are used for initiating aza-Cope/Mannich reactions by ring-opening of oxazolidines, often with diethylaluminum chloride or the boron trifluoride–diethyl ether complex. These reagents require anhydrous solvents, often dichloromethane at cryogenic temperatures (−20 to 0°) under an inert atmosphere.

With regard to the choice of carbonyl component, a wide variety of aliphatic and aromatic aldehydes work successfully. There is no requirement for using anhydrous solutions of monomeric formaldehyde; commercially available polymeric paraformaldehyde performs well. As discussed previously, sterically demanding aldehydes or ketones are less successful for direct condensation to generate iminium ions; oxazolidine formation, followed by rearrangement on treatment with a protic or Lewis acid, or under basic conditions, is preferable.

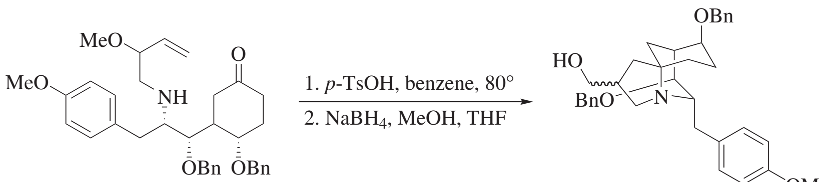
The limited examples of the base-mediated aza-Cope/Mannich reaction are accomplished by adding potassium hydride, potassium hydroxide, or triphenylmethylpotassium to a cyanomethyl amine or oxazolidine in tetrahydrofuran at room temperature under an inert atmosphere. The reaction is insensitive to the order of reagent addition, with the amine solution typically added to a potassium hydride suspension and the triphenylmethylpotassium solution added to the amine solution for experimental convenience. As potassium hydride is typically supplied as a suspension in mineral oil, the oil is removed by careful washing with hexane. The triphenylmethylpotassium reagent is generated and used as a tetrahydrofuran solution.[107] Because of the sensitive nature of the reagents, both an anhydrous solvent and inert atmosphere are essential for the success of the reaction. The reactions are also carried out at room temperature, with no requirement for cooling during addition.

EXPERIMENTAL PROCEDURES



3-Acetyl-1-benzylpyrrolidine [Condensation of an Amino Alcohol with Paraformaldehyde].[31] A mixture of 1-benzylamino-2-methylbut-3-en-2-ol (450 mg, 2.35 mmol), paraformaldehyde (78 mg, 2.60 mmol), CSA (495 mg, 2.13 mmol), and anhydrous benzene (5 mL) was heated at reflux for 10 hours under Ar. After the reaction mixture was cooled to room temperature, 1 N aqueous NaOH (3 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Purification by bulb-to-bulb distillation

(oven temperature 95–105°, 0.4 mmHg) gave the title product as a colorless oil (425 mg, 89%), which was >95% pure by GC analysis. A specimen was purified by preparative GC to yield an analytical sample: IR (film) 1712 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.40–7.20 (m, 5H), 3.62 (br s, 2H), 3.20–3.05 (m, 1H), 2.90–2.75 (m, 1H), 2.75–2.45 (m, 3H), 2.15 (s, 3H), 2.20–1.95 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 208.8, 139.0, 128.7, 128.3, 127.1, 60.2, 55.7, 53.9, 50.5, 28.5, 26.6; CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{13}H_{18}NO$, 204.1388; found, 204.1380.

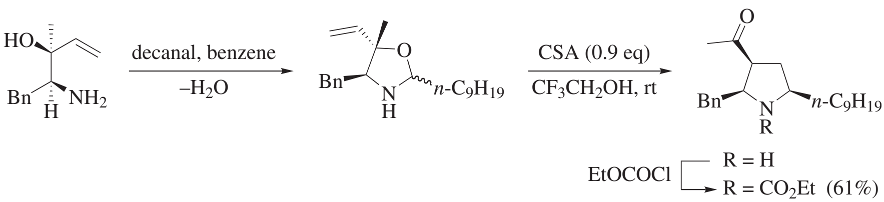


104

(63%) 2:1 dr

[7,9-Bis(benzyloxy)-6-(4-methoxybenzyl)-5-azatricyclo-[6.3.1.0^{1,5}]dodec-3-yl]methanol [Condensation of an Amino Ether with a Ketone].[40] A flask equipped with a Dean–Stark apparatus was charged with keto amine **104** (230 mg, 0.41 mmol), and a solution of benzene (20 mL) and p-TsOH (94 mg, 0.50 mmol) was added in a single portion. The solution was slowly heated to reflux under N_2 over 30 minutes, and then maintained at that temperature for 3 hours. The solution was cooled to room temperature and saturated aqueous $NaHCO_3$ solution was added. The organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic phases were washed with water (10 mL), brine (10 mL), dried ($MgSO_4$), and then concentrated under reduced pressure. The residue was dissolved in THF (20 mL) and transferred by cannula into a solution of $NaBH_4$ (30 mg, 0.79 mmol) in MeOH (10 mL) at −78° over 10 minutes. The resulting solution was allowed to warm to room temperature. Ice water (10 mL) was added, the aqueous layer was separated and then extracted with Et_2O. The combined organic phases were washed with water (10 mL) and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Column chromatography (silica gel, CH_2Cl_2/MeOH/NH_4OH 24:1:1) gave the title products as a separable mixture of diastereomers in order of elution (major α: 91 mg, 42%; minor β: 41 mg, 21%): IR (film) 3396, 2928 cm^{-1}; α isomer: $[\alpha]^{25}_D + 73.8$ (c 0.058, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.24 (m, 10H), 7.07 (d, J = 8.5 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 4.46 (d, J = 11.7 Hz, 1H), 4.43 (s, 2H), 4.16 (d, J = 11.7 Hz, 1H), 3.81 (s, 3H), 3.67 (dd, J = 9.9, 5.2 Hz, 1H), 3.56 (dd, J = 15.8, 5.8 Hz, 1H), 3.37–3.25 (m, 2H), 3.17 (br s, 1H), 3.08 (dd, J = 9.3, 4.0 Hz, 1H), 2.99–2.80 (m, 4H), 2.50 (s, 1H), 2.33 (br s, 1H), 2.03–1.77 (m, 5H), 1.70 (dd, J = 12.2, 9.4 Hz, 1H), 1.60–1.48 (m, 1H), 1.47 (dd, J = 12.2, 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 139.3, 139.2, 131.9, 130.5, 128.7, 127.8, 127.7, 114.0, 77.6, 75.7, 74.9, 71.4, 70.5, 67.8,

64.1, 60.8, 59.4, 55.5, 54.6, 51.8, 43.3, 36.7, 36.6, 36.0, 27.8, 27.5. β isomer: $[\alpha]^{25}{}_{D} + 42.5$ (*c* 0.050, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.24 (m, 10H), 7.07 (d, $J = 8.6$ Hz, 2H), 6.80 (d, $J = 8.6$ Hz, 2H), 4.54 (d, $J = 11.6$ Hz, 1H), 4.48 (d, $J = 12.1$ Hz, 1H), 4.42 (d, $J = 12.1$ Hz, 1H), 4.16 (d, $J =$ 11.6 Hz, 1H), 3.80 (s, 3H), 3.68 (dd, $J = 9.8$, 4.3 Hz, 1H), 3.57–3.43 (m, 3H), 3.33 (br s, 1H), 3.07 (dd, $J = 12.9$, 10.3 Hz, 1H), 2.96–2.89 (m, 2H), 2.84 (dd, $J = 13.0$, 4.8 Hz, 1H), 2.52 (s, 1H), 2.25 (m, 1H), 2.12–1.95 (m, 2H), 1.95–1.70 (m, 4H), 1.55–1.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 139.3, 139.2, 131.9, 130.5, 130.4, 128.7, 128.6, 127.7, 127.5, 114.1, 76.3, 74.9, 71.4, 70.7, 68.5, 59.2, 58.9, 55.5, 52.1, 43.4, 36.9, 36.1, 36.0, 31.4, 30.0, 27.2, 23.5, 23.0; EI-HRMS (m/z): $[M + H]^+$ calcd for $C_{34}H_{41}NO_4$, 526.2957; found, 526.2961.

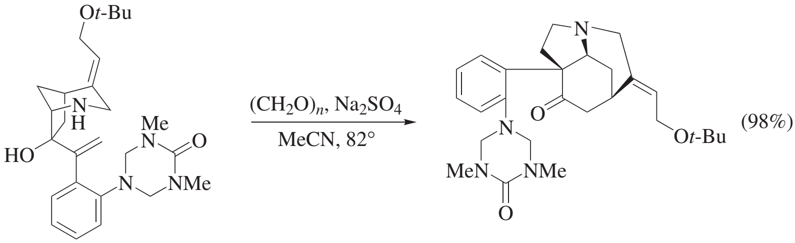


(2*S*,3*S*,5*R*)-3-Acetyl-2-benzyl-1-(ethoxycarbonyl)-5-nonylpyrrolidine [Rearrangement of a Vinyl Oxazolidine].[43] A mixture of (3*S*, 4*S*)-4-amino-3-methyl-5-phenylpent-1-en-3-ol (300 mg, 1.57 mmol), freshly distilled decanal (258 mg, 1.57 mmol), and dry benzene (2 mL) was heated at reflux for 2 hours under Ar in a Soxhlet apparatus containing calcium carbide. The mixture was concentrated under reduced pressure at room temperature to provide the crude oxazolidine as a 3:l mixture of stereoisomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.25 (m, major and minor), 5.85 (dd, $J = 17.9$, 10.7 Hz, minor), 5.83 (dd, $J = 17.3$, 10.7 Hz, major), 5.31 (dd, $J = 7.2$, 1.5, Hz, minor), 5.28 (dd, $J = 16.1$, 1.4 Hz, major), 5.08 (dd, $J = 10.7$, 1.2 Hz, major and minor), 4.85 (t, $J = 5.7$ Hz, minor), 4.57 (t, $J = 5.3$ Hz, major), 3.31 (dd, $J = 9.5$, 4.8 Hz, major and minor), 2.84–2.71 (m, major and minor), 2.53 (br s, major and minor), 1.72–1.66 (m, major and minor), 1.50–1.42 (m, major and minor), 1.38–1.26 (m, major and minor), 0.93 (t, $J = 7.0$ Hz, minor), 0.92 (t, $J = 6.9$ Hz, minor); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4 (minor), 142.5 (major), 139.2 (minor), 138.9 (major), 129.0 (minor), 128.8 (major), 128.5 (major), 128.3 (minor), 126.4 (major), 126.2 (minor), 113.0 (minor), 112.8 (major), 90.7 (major), 90.4 (minor), 82.5 (minor), 81.4 (major), 68.3 (major), 66.0 (minor), 43.9, 36.3, 35.5, 35.4, 35.2, 31.9, 29.6, 29.55, 29.5, 29.4, 29.35, 29.3, 29.27, 29.2, 29.1, 25.4, 25.0 (major), 22.6 (major), 22.0 (minor), 19.8 (minor), 14.1.

Camphorsulfonic acid (350 mg, 1.49 mmol) was added to a solution of the crude oxazolidine isomers in CF_3CH_2OH (4 mL) and the mixture was maintained at room temperature for 40 hours under Ar. After concentration

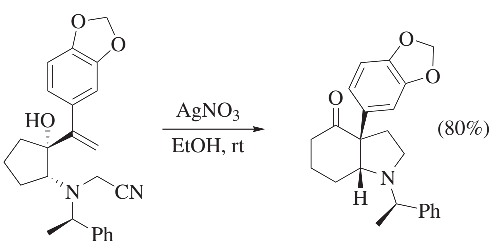
under reduced pressure, the residue was dissolved in $CHCl_3$ (100 mL), and the solution was washed with 1 N aqueous NaOH and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude pyrrolidine products were dissolved in $CHCl_3$ (16 mL) and then ethyl chloroformate (0.23 mL, 2.4 mmol) and solid $NaHCO_3$ (1.30 g, 15.0 mmol) were added. The resulting mixture was stirred at room temperature for 2 hours under Ar, filtered, and then concentrated under reduced pressure. Purification by column chromatography (silica gel, hexanes/EtOAc 15:1) gave the title product (383 mg, 61%, 77% ee), a mixture of three additional stereoisomers (26%), and recovered starting material (2%): $[\alpha]^{25}{}_{D} - 26.7$, $[\alpha]^{25}{}_{577} - 26.1$, $[\alpha]^{25}{}_{546} - 29.0$, $[\alpha]^{25}{}_{435} - 34.2$, $[\alpha]^{25}{}_{405} - 29.7$($c$ 1.0, $CHC1_3$); IR (film) 2954, 1708, 1686, 1410, 1281 cm^{-1}; ^{1}H NMR (500 MHz, $C_6D_5CD_3$, 100°) δ 7.17–6.96 (m, 5H), 4.53 (dd, $J = 13.3$, 7.1 Hz, 1H), 3.96 (m, 2H), 3.65 (m, 1H), 2.72 (dd, $J = 13.8$, 5.8 Hz, 1H), 2.61 (dd, $J = 13.8$, 7.5 Hz, 1H), 2.53 (dt, $J = 12.7$, 7.0 Hz, 1H), 2.22 (m, 1H), 1.82 (dt, $J = 13.0$, 7.0 Hz, 1H), 1.46 (s, 3H), 1.36–1.26 (m, 15H), 1.01 (t, $J = 7.0$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, $C_6D_5CD_3$, 100°) δ 203.8, 155.2, 139.3, 130.6, 128.5, 126.7, 61.6, 60.9, 58.1, 54.6, 39.3, 37.2, 32.5, 32.2, 30.3, 30.2, 30.0, 29.9, 26.7, 23.1, 20.0, 14.8, 14.2; CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{25}H_{40}NO_3$, 402.3008; found, 402.3001. Anal. Calcd for $C_{25}H_{39}NO_3$: C, 74.76; H, 9.79; N, 3.49. Found: C, 74.67; H, 9.83; N, 3.43.

Diagnostic characterization data for the three minor stereoisomers follows. (2S,3R,5R)-3-Acetyl-2-benzyl-l-ethoxycarbonyl-5-nonylpyrrolidine: ^{1}H NMR (500 MHz, $C_6D_5CD_3$, 100°) δ 7.10–6.96 (m, 5H), 4.46 (dt, $J = 8.9$, 4.4 Hz, 1H), 4.12–4.02 (m, 2H), 3.98–3.93 (m, 1H), 3.21 (dd, $J = 9.2$, 4.1 Hz, 1H), 2.71 (dt, $J = 7.0$, 4.8 Hz, 1H), 2.66 (dd, $J = 13.2$, 9.0 Hz, 1H), 1.94 (ddd, $J = 11.9$, 7.6, 5.2 Hz, 1H), 1.80–1.73 (m, 1H), 1.52 (s, 3H), 1.50 (m, 1H), 1.34–1.24 (m, 15H), 1.10 (t, $J = 7.0$ Hz, 3H), 0.90 (t, $J = 6.9$ Hz, 3H); CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{25}H_{40}NO_3$, 402.3008; found, 402.3009. (2R, 3S, 5R)-3-Acetyl-2-benzy1-l-(ethoxycarbonyl)-5-nonylpyrrolidine: ^{1}H NMR (500 MHz, $C_6D_5CD_3$, 100°) δ 7.11–6.96 (m, 5H), 4.58 (dt, $J = 8.2$, 3.1 Hz, 1H), 4.18–4.05 (m, 2H), 3.71–3.66 (m, 1H), 3.30–3.24 (m, 1H), 2.56 (dd, $J = 13.2$, 8.9 Hz, 1H), 2.49 (dt, $J = 9.1$, 2.4 Hz, 1H), 2.07–2.05 (m, 1H), 1.97 (dt, $J = 13.2$, 2.4 Hz, 1H), 1.70 (dt, $J = 13.0$, 4.4 Hz, 1H), 1.54 (s, 3H), 1.34–1.24 (m, 15H), 1.13 (t, $J = 7.0$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 3H); CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{25}H_{40}NO_3$, 402.3008; found, 402.3008. (2R, 3R, 5R)-3-Acetyl-2-benzyl-1-(ethoxycarbonyl)-5-nonylpyrrolidine: ^{1}H NMR (500 MHz, $C_6D_5CD_3$, 100°) δ 7.20–6.95 (m, 5H), 4.45–4.40 (m, 1H), 4.10–4.00 (m, 2H), 3.75–3.65 (m, 1H), 3.00–2.88 (m, 1H), 2.86 (dt, $J = 13.2$, 6.9 Hz, 1H), 2.66 (dd, $J = 13.6$, 8.5 Hz, 1H), 2.25 (dt, $J = 12.7$, 8.7 Hz, 1H), 1.42 (dd, $J = 12.9$, 6.0 Hz, 1H), 1.38 (s, 3H), 1.32–1.24 (m, 16H), 1.11 (t, $J = 7.2$ Hz, 3H), 0.88 (t, $J = 6.9$ Hz, 3H); CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{25}H_{40}NO_3$, 402.3008; found, 402.2993.



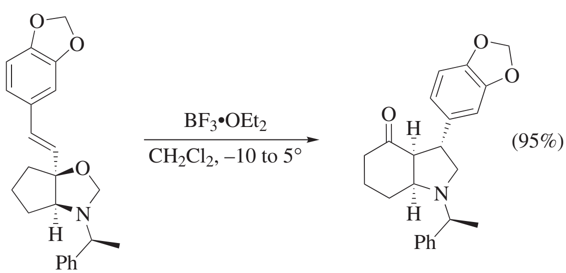
90

(1*R*,7*R*,8*S*)-2-((2-*tert*-Butoxy)-1-(*E*)-ethylidene)-7-[2-[5-(1,3-dimethylhexahydro-2-oxa-1,3,5-triazinyl)]phenyl]-4-azatricyclo[5.2.2.0^{4,8}]undecan-11-one [Ring-Enlarging Annulation of an Amino Alcohol].[32,33] A mixture of the azabicyclooctane **90** (1.60 g, 3.5 mmol), Na_2SO_4 (4.90 g, 35 mmol), paraformaldehyde (320 mg, 11 mmol), and MeCN (40 mL) was heated at reflux under Ar for 10 minutes and then concentrated under reduced pressure. Column chromatography (silica gel, $CHCl_3$/MeOH 19:1) gave the title product as a colorless solid (1.60 g, 98%): mp 151–152° (EtOAc/hexane); $[\alpha]^{25}_D + 39.0$ (*c* 1.1, $CHCl_3$); IR (film) 2973, 2936, 2874, 1690, 1652, 1520, 1491, 1420, 1306, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, $J = 7.9$ Hz, 1H), 7.30–7.21 (m, 2H), 7.19 (dd, $J = 7.5$, 1.2 Hz, 1H), 5.43 (t, $J = 6.2$ Hz, 1H), 4.11 and 4.52 (AB, $J_{AB} = 12.2$ Hz, 2H), 3.98 (app dd, $J = 11.2$, 2.2 Hz, 1H), 3.93–3.91 (m, 2H), 3.80 (app s, 1H), 3.54 (app d, $J = 15.2$ Hz, 1H), 3.51 (app dd, $J = 12.2$, 2.2 Hz, 1H), 3.26–3.23 (m, 1H), 3.21 (app d, $J = 5.0$ Hz, 1H), 3.00–2.94 (m, 2H), 2.92 (s, 3H), 2.91–2.86 (m, 1H), 2.76 (s, 3H), 2.73 (app d, $J = 5.8$ Hz, 1H), 2.44 (app td, $J = 14.7$, 2.1 Hz, 1H), 2.10–2.03 (m, 2H), 1.87 (app d, $J = 13.9$ Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.1, 155.8, 146.7, 140.4, 138.6, 128.2, 128.1, 127.6, 125.9, 123.6, 73.1, 69.4, 68.9, 68.7, 61.8, 57.1, 54.0, 53.8, 46.9, 39.1, 32.7, 32.5, 31.8, 27.4, 25.9; CI-HRMS (m/z): [M + H] calcd for $C_{27}H_{39}N_4O_3$, 467.3020; found, 467.2968. Anal. Calcd for $C_{27}H_{38}N_4O_3$: C, 69.50; H, 8.21; N, 12.0. Found: C, 69.54; H, 8.19; N, 11.90.



105

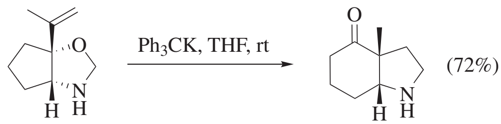
(3aS,7aR)-1-[(R)-α-Methylbenzyl]-3a-[3,4-(methylenedioxy)phenyl]-2,3,3a,4,5,6,7,7a-octahydro-4-(1H)-indolone [Ring-Enlarging Annulation of a Cyanomethylamino Alcohol].[48] A solution of cyanomethyl amine **105** (2.18 g, 5.58 mmol) in EtOH (40 mL) was deoxygenated at room temperature by evacuating the reaction flask and refilling it with Ar five times. Solid $AgNO_3$ (950 mg, 5.59 mmol) was added, the resulting mixture was stirred for 3 hours at room temperature under Ar, and then filtered through Celite. The Celite was washed with EtOH (10 mL), the combined filtrates were concentrated, 1 M aqueous NaOH was added, and the resulting mixture was extracted with a hexane/EtOAc (4:1) mixture. The combined organic phase was dried (Na_2SO_4) and then evaporated under reduced pressure. Column chromatography (silica gel, hexane/EtOAc/NEt_3 30:1:0.1) gave the title product as a colorless crystalline solid (1.63 g, 80%): mp 105–106°, $[\alpha]^{23}_{D} + 129$, $[\alpha]^{23}_{578} + 136$, $[\alpha]^{23}_{546} + 163$, $[\alpha]^{23}_{435} + 360$ (c 1.02, MeOH); IR ($CHCl_3$) 2948, 2878, 1711, 1489, 1240, 1037, 933 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40–7.20 (m, 5H), 6.80–6.65 (m, 3H), 5.94 (app s, 2H), 4.14 (q, $J = 6.7$ Hz, 1H), 3.70 (br s, 1H), 3.83 (ddd, $J = 4.6, 7.9, 12.0$ Hz, 1H), 2.55–1.20 (m, 9H), 1.34 (d, $J = 6.7$ Hz, 3H); CI-MS (m/z): 364, 260, 105. HCl salt: Anal. Calcd for $C_{23}H_{26}ClNO_3$: C, 69.07; H, 6.55; Cl, 8.89; N, 3.50. Found: C, 68.85; H, 6.58; Cl, 8.95; N, 3.46.



106

(3R, 3aS,7aS)-N-[(1S)-Methylbenzyl]-3-(1,3-benzodioxol-5-yl)-2,3,3a,4,5,6,7,7a-octahydro-4-(1H)-indolone [Ring-Enlarging Annulation of a Vinyl Oxazolidine].[60] To a solution of oxazolidine **106** (166 mg, 0.46 mmol) in CH_2Cl_2 (10 mL), which had been filtered through basic alumina (Brockmann activity I), was added $BF_3 \bullet OEt_2$ (0.16 g, 1.1 mmol) at −10° under Ar. The cooling bath was changed to an ice bath (5°), and after 2 hours at 5°, saturated aqueous $NaHCO_3$ solution (3 mL) was added. The aqueous layer was then extracted with $CHCl_3$ and the combined organic phase was dried (K_2CO_3). Evaporation under reduced pressure gave the product as a yellow solid (157 mg, 95%). An analytically pure sample was prepared by recrystallization from hexanes/$CHCl_3$ (1:l) as slightly yellow needles: mp 117–118°; $[\alpha]^{25}_{D} + 34.6$, $[\alpha]^{25}_{577} + 34.6$, $[\alpha]^{25}_{546} + 38.1$, $[\alpha]^{25}_{435} + 60.2$, $[\alpha]^{25}_{405} + 65.1$ (c 0.65, $CHC1_3$); IR (KBr) 2934,

1702, 1492, 1248, 1034, 927 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.23 (m, 5H), 6.74 (d, J = 1.0 Hz, 1H), 6.70 (d, J = 7.9 Hz, 1H), 6.66 (dd, J = 8.0, 1.5 Hz, 1H), 5.91 (s, 2H), 3.82 (q, J = 6.6 Hz, 1H), 3.59 (app q, J = 8.1 Hz, 1H), 3.48−3.44 (m, 1H), 3.12 (app t, J = 8.7 Hz, 1H), 2.82 (app t, J = 7.7 Hz, 1H), 2.54 (app t, J = 8.9 Hz, 1H), 2.44−2.27 (m, 1H), 1.97−1.58 (m, 2H), 1.36 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 211.2, 147.6, 145.9, 144.6, 136.6, 128.0, 127.2, 126.7, 120.4, 107.9, 107.6, 100.7, 63.1, 59.6, 58.7, 56.5, 43.8, 39.4, 26.6, 26.3, 12.8; CI-HRMS (m/z): $[M + H]^+$ calcd for $C_{23}H_{26}NO_3$, 363.1834; found, 363.1826. Anal. Calcd for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93; N, 3.85. Found: C, 76.00; H, 6.96; N, 3.90.



107

(3a*R,7a*R**)-3a-Methylhexahydro-2,3,3a,4,5,6,7,7a-octahydro-4-(1*H*)-indolone [Base-Promoted Aza-Cope/Mannich Reaction].[62]** To a solution of oxazolidine **107** (58 mg, 0.38 mmol) in THF (7.6 mL) was added a solution of triphenylmethylpotassium (0.5 mL, 0.90 M solution in THF, 0.46 mmol)[107] at room temperature under Ar. After the mixture had stirred for 10 minutes, MeOH (0.20 mL) was added, followed by brine (10 mL). The aqueous layer was extracted with $CHCl_3$, the combined organic extracts were dried (K_2CO_3), and then concentrated under reduced pressure. Column chromatography (silica gel, CH_2Cl_2/MeOH/NH_4OH 9:1:0.1) gave the title product as a light yellow oil (42 mg, 72%): IR (film) 3344, 1702, 1456 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.15 (m, 1H), 2.94 (m, 2H), 2.58 (ddd, J = 5.8, 8.4, 12.8 Hz, 1H), 2.53−2.27 (m, 2H), 2.12−1.70 (m, 4H), 1.61 (br s, 1H), 1.43 (ddd, J = 6.5, 8.9, 12.7 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.9, 67.1, 55.1, 43.4, 38.2, 35.2, 26.4, 22.2, 21.7; EI-HRMS (m/z): $[M + H]^+$ calcd for $C_9H_{15}NO$, 153.1154; found, 153.1157.

TABULAR SURVEY

The tabular survey includes all examples of the aza-Cope/Mannich reaction found in the literature through March 2009 identified by searching *Chemical Abstracts*.

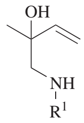
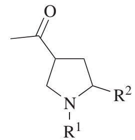
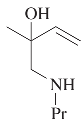
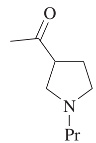
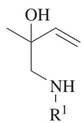
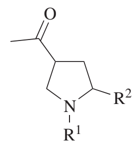
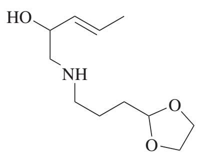
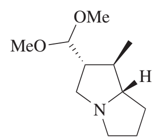
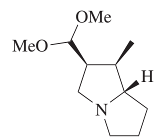
The tables are divided based on the nature of the reaction precursor. Tables 1–3 summarize the aza-Cope/Mannich reaction of amino alcohols, amino ethers, and vinyl oxazolidines, respectively. Tables 4–6 present the ring-enlarging annulation reactions of amino alcohols, cyanomethylamino alcohols, and vinyl oxazolidines, respectively. Table 7 contains examples of the base-promoted aza-Cope/Mannich reaction.

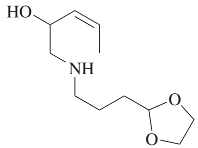
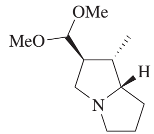
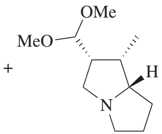
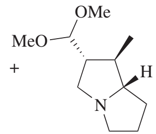
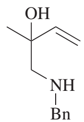
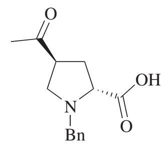
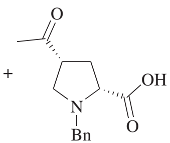
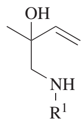
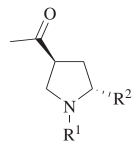
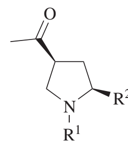
Entries within the tables are arranged in order of increasing number of carbon atoms in the reactant containing the 1-aminobut-3-en-2-ol functionality.

The following abbreviations are used in the tables:

CSA	camphorsulfonic acid
p-TSA	*p*-toluenesulfonic acid
PMP	*p*-methoxyphenyl

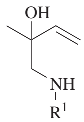
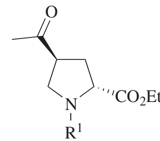
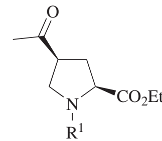
TABLE 1. CONDENSATION OF AMINO ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-12} 	R^2CHO, CSA (0.9 eq), benzene, reflux	 R^1 / R^2 Me / 3-pyridyl (84) Bn / 2-furyl (95) Bn / 3-pyridyl (91) Bn / Ph (94)	4, 31
C_8 	$(CH_2O)_n$, CSA (0.9 eq), ethanol, reflux, 24 h	 (90)	31
C_{11} 	R^2CHO, CSA (0.9 eq), toluene, reflux	 R^1 / R^2 / Time (h) Ph / H / 1.5 (66) 4-FC_6H_4 / n-C_5H_{11} / 19 (83) 2-ClC_6H_4 / H / 1 (74) Ph / Ph / 28 (56)	31
	HCl, MeOH, 65°, 6 h	 (84) +  (6)	28

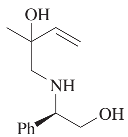
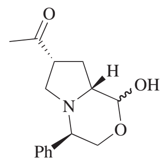
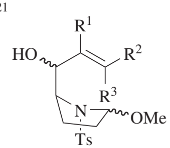
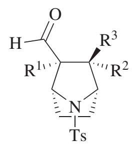
Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
	HCl, MeOH, 115°, 12 h, sealed tube	 (42) +  (15) +  (20)	28
C_{12} 	$OHCCO_2H{\bullet}H_2O$, MeOH, 48 h, rt	 (51–61) +  (13–3)	57
C_{12-18} 	R^2CHO, CSA (1.0 eq), $CuSO_4$, MeCN, microwaves	 **I** +  **II**	56

R^1	R^2	Temp (°)	Time (min)	**I + II**	**I:II**
Bn	Et	90	15	(84)	3:1
Bn	Et	60	60	(63)	3:1
Bn	Et	60	5	(22)	3:1
Bn	(*E*)-CH=CHPh	90	15	(84)	1:1
Ph_2CH	Et	90	35	(84)	5:1
Ph_2CH	Et	60	150	(82)	8:1
Ph_2CH	(*E*)-CH=CHPh	90	35	(75)	2:1
Ph_2CH	(*E*)-CH=CHPh	60	360	(65)	5:1

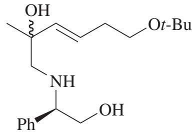
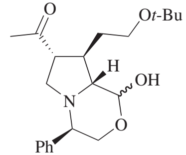
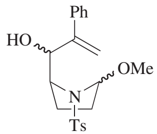
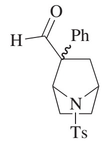
TABLE 1. CONDENSATION OF AMINO ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-18} 	$EtO_2CCH(OEt)_2$, CSA (1.0 eq), $CuSO_4$, MeCN, microwaves	 **I** +  **II**	56

R^1	Temp (°)	Time (min)	I + II	I:II
Bn	90	15	(74)	2:1
Ph_2CH	90	30	(79)	2:1
Ph_2CH	60	60	(84)	5:1

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	OHCCHO, *p*-TsOH, H_2O, THF, rt, 40 h	 (45)	24, 67, 70
C_{15-21} 	$SnCl_4$ (1 eq), CH_2Cl_2		26

R^1	R^2	R^3	Temp (°)	Time	
H	H	H	20	14.5 h	(32)
Me	H	H	0	8 min	(81)
Me	H	Me	0	8 min	(62)
Me	Me	H	0	8 min	(61)
Ph	H	H	0	8 min	(96)
SPh	H	H	0	1 min	(11)

C_{19} 	OHCCHO, 1 N HCl, H_2O, THF, rt, 72 h	 (45)	24, 52
C_{21} 	See table		26

Acid (eq)	Solvent	Temp	Time	
CSA (0.08)	MeCN	80°	16 h	(0)
$TiCl_4$ (1)	CH_2Cl_2	0°	8 min	(31)
$Sc(OTf)_3$ (0.1)	CH_2Cl_2	rt	17 h	(0)
$SnCl_4$ (2)	CH_2Cl_2	0°	8 min	(96)
$SnCl_4$ (1)	CH_2Cl_2	0°	8 min	(96)
$SnCl_4$ (0.1)	CH_2Cl_2	rt	15 h	(—)

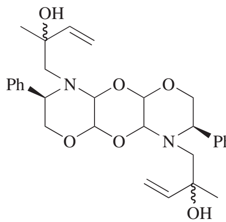
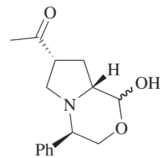
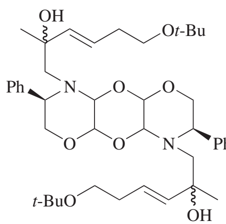
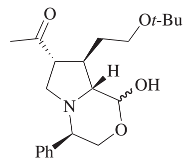
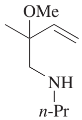
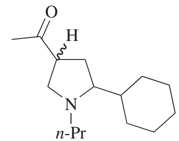
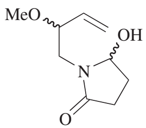
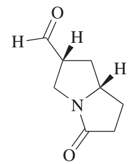
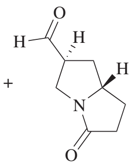
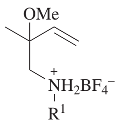
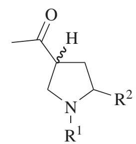
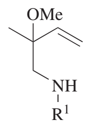
C_{30} 	*p*-TsOH, H_2O, THF, rt, 48 h	 (55)	67, 70
C_{42} 	1 N HCl, H_2O, THF, rt, 72 h	 (37)	52

TABLE 2. CONDENSATION OF AMINO ETHERS

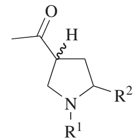
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	c-$C_6H_{11}CHO$, CSA (0.1 eq), benzene, reflux, 24 h	 (90)	4, 31
	HCO_2H, rt, 18 h	 (48) +  (10)	63
C_{9-12} 	R^2CHO, benzene, reflux		4, 31

R^1	R^2	Time (h)	
n-Pr	Ph	5	(87)
n-Pr	c-C_6H_{11}	24	(95)
n-Pr	n-C_6H_{13}	24	(97)
n-Pr	(E)-$Me_2C{=}CHCH_2CMe{=}CHCH_2$	24	(90)
c-C_6H_{11}	n-C_6H_{13}	24	(95)

C_{9-13}



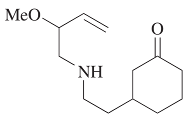
R^2CHO, CSA (0.9 eq), benzene, reflux



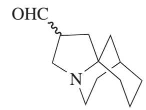
4, 31

R^1	R^2	Time (h)	
n-Pr	Ph	24	(85)
n-Pr	*c*-C_6H_{11}	24	(84)
Bn	Ph	24	(54)
Bn	Ph	72	(89)
Bn	2-furyl	24	(57)

C_{13}



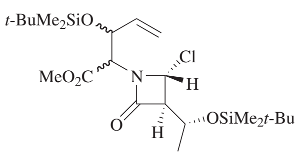
p-TSA, benzene, reflux, 18 h



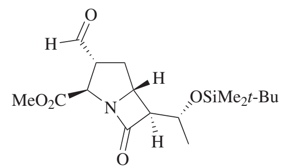
(72) 2:1 dr

39

C_{23}



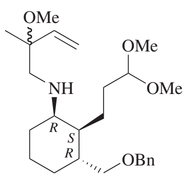
$AgBF_4$, CH_2Cl_2, –78°



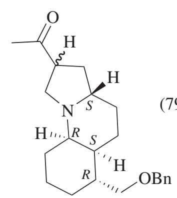
(33)

64

C_{25}



p-TSA, benzene, 80°, 6 h



(79) ~3:2 mixture of epimer

41

TABLE 2. CONDENSATION OF AMINO ETHERS (*Continued*)

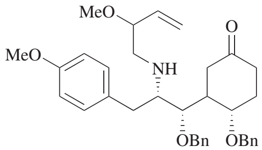
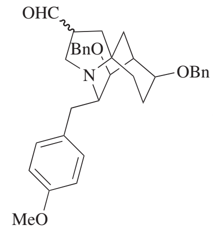
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{35}			
	*p*-TSA, benzene, reflux, 3 h	 (63) 2:1 dr	40

TABLE 3. REARRANGEMENT OF VINYL OXAZOLIDINES

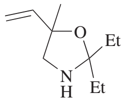
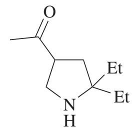
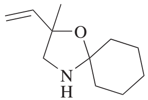
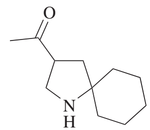
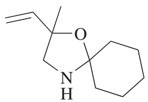
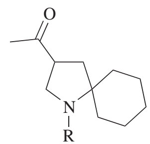
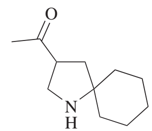
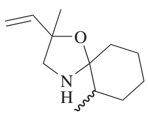
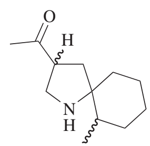
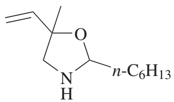
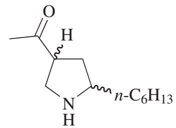
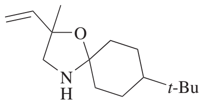
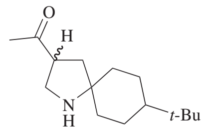
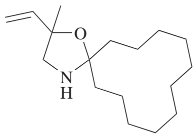
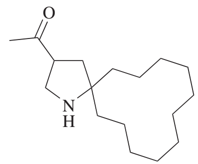
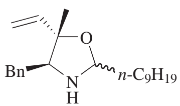
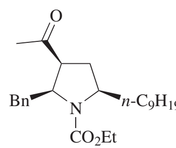
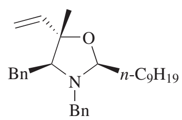
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	CSA, benzene, reflux, 24 h	 (9)	31, 59
C_{11} 	CSA, benzene, reflux, 24 h	 (69)	31, 59
	RX, solvent, reflux, 24 h	 **I** +  **II**	
	R / X / Solvent	**I** / **II**	
	Me / I / benzene	(54) / (17)	31, 59
	Me / OTs / benzene	(49) / (17)	59
	n-C_6H_{13} / I / DMF	(45) / (9)	59
	n-C_8H_{17} / I / DMF	(48) / (21)	31, 59
C_{12} 	CSA, benzene, reflux, 24 h	 (55) mixture of 4 isomers	31, 59

TABLE 3. REARRANGEMENT OF VINYL OXAZOLIDINES (*Continued*)

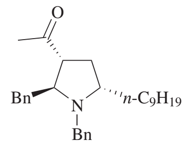
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	CSA, benzene, reflux, 24 h	 (65)	31, 59
C_{15} 	CSA, benzene, reflux, 24 h	 (70) 92:8 dr	31, 59
C_{17} 	CSA, benzene, reflux, 24 h	 (13)	31
C_{22} 	1. CSA, CF_3CH_2OH, rt 2. EtOCOCl, $NaHCO_3$	 (61) 80% ee	43

C_{29}



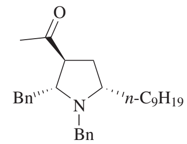
97% ee

See table



I

+

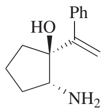
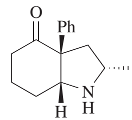
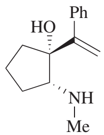
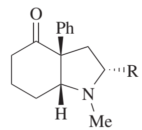
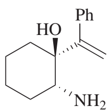
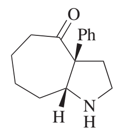
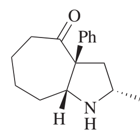
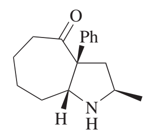
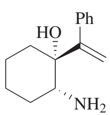


II

43

Acid (eq)	Solvent	Temp	**I**, % ee	**II**, % ee
CSA (0.95)	CF_3CH_2OH	rt	(60), 86	(7), —
TFA	TFA	72°	(68–78), 78–88	(6–10), 78–80
Et_2AlCl (0.5)	toluene	rt	(48), 97	(15), 28
Et_2AlCl (0.5)	toluene	85°	(16), 85	(67), 62

TABLE 4. RING-ENLARGING ANNULATION OF AMINO ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	MeCHO (4 eq), CSA, ethanol, reflux, 4 h	 (66)	29, 55
C_{14} 	RCHO (2 eq), CSA, ethanol, reflux, 5 h	 R: Me (81); n-C_6H_{13} (77)	29, 55
	$(CH_2O)_n$, CSA, benzene, reflux, 22 h	 (93)	50, 68
	MeCHO, CSA, benzene, reflux, 4 h	 (50) +  (6) **I** **II**	50
	MeCHO, CSA, benzene, reflux, 4 h	**I** (54) + **II** (2)	50

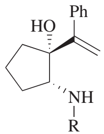
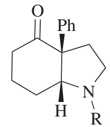
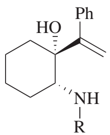
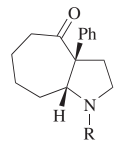
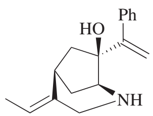
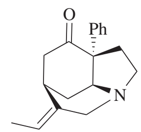
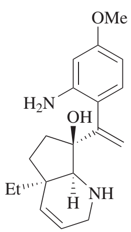
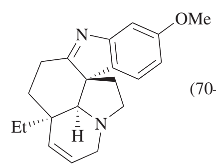
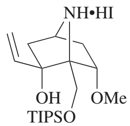
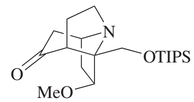
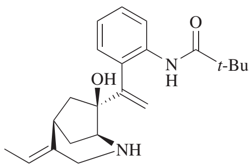
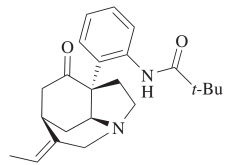
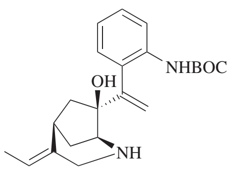
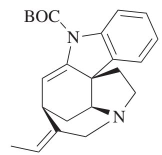
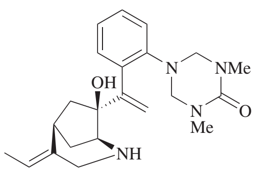
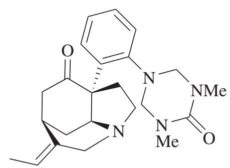
C_{14-26} 	$(CH_2O)_n$, ethanol, reflux, 20 h	 R — Me (78); $CHPh_2$ (78)	29, 58 29
C_{14-27} 	$(CH_2O)_n$, CSA, benzene, reflux, 22 h	 R — H (>90); $CHPh_2$ (96)	50, 68
C_{17} 	$(CH_2O)_n$, CSA, Na_2SO_4, MeCN, reflux	 (90)	38
C_{19} 	1. $(CH_2O)_n$, Na_2SO_4, toluene, rt, 1 h 2. reflux, 6 h	 (70–90)	65

TABLE 4. RING-ENLARGING ANNULATION OF AMINO ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{19} 	$(CH_2O)_n$, toluene, MeCN, 80°, 30 min	 (94)	45
C_{22} 	$(CH_2O)_n$, CSA, Na_2SO_4, MeCN, reflux	 (88)	37, 38
	$(CH_2O)_n$, Na_2SO_4, MeCN, reflux	 (60)	38
	$(CH_2O)_n$, Na_2SO_4, MeCN, reflux	 (98)	38

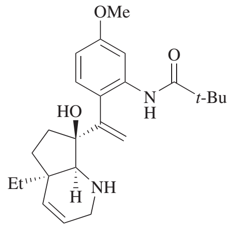
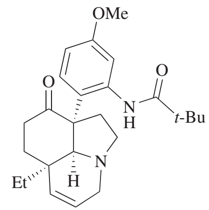
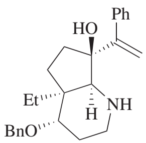
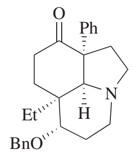
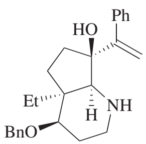
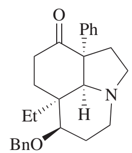
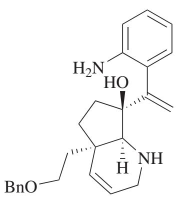
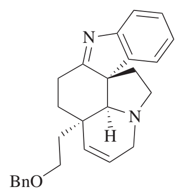
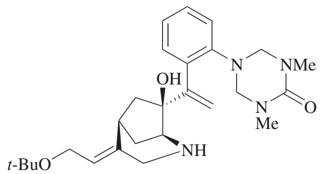
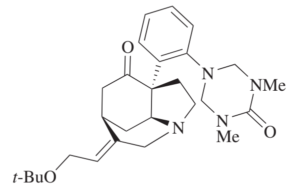
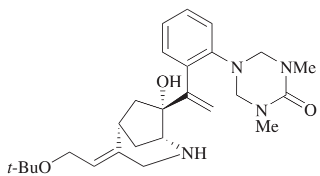
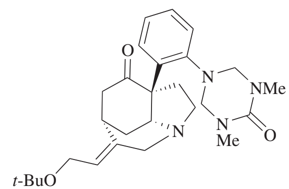
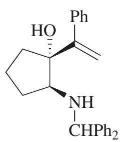
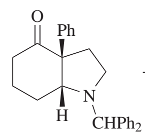
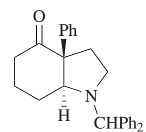
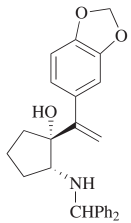
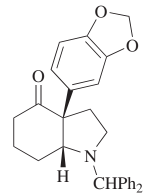
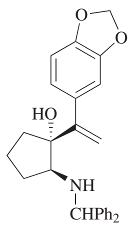
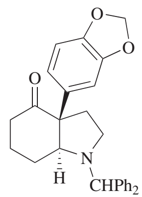
C_{24}		$(CH_2O)_n$, CSA, benzene, reflux, 2 h	 (96)	65
C_{25}		$(CH_2O)_n$, CSA, benzene, reflux, 4 h	 (83)	95
		$(CH_2O)_n$, CSA, benzene, reflux, 4 h	 (86)	95
		1. $(CH_2O)_n$, Na_2SO_4, benzene, rt, 1 h 2. CSA, benzene, reflux, 2.5 h	 (100)	36

TABLE 4. RING-ENLARGING ANNULATION OF AMINO ALCOHOLS (*Continued*)

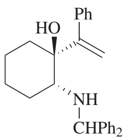
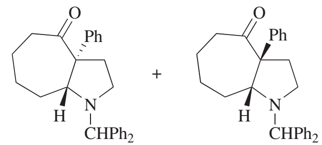
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{26}			
	$(CH_2O)_n$, Na_2SO_4, MeCN, reflux	 (98)	32, 33
	$(CH_2O)_n$, Na_2SO_4, MeCN, reflux	 (98)	33, 75
	$(CH_2O)_n$, CSA, 20 h	 I +  II	29

Solvent	Concn (M)	Temp (°)	I + II	I:II
benzene	0.15	80	(82)	3:1
THF	0.08–0.01	65	(—)	1.5:1
2% aq THF	0.08	65	(—)	3.8:1
EtOH	0.15	78	(—)	11:1
DMSO	0.15	83	(68)	>30:1

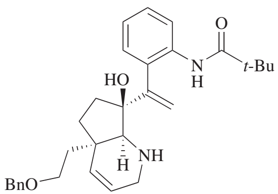
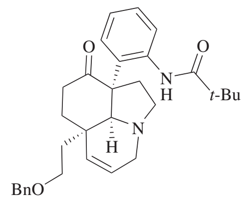
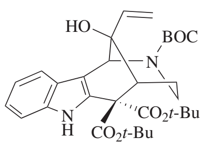
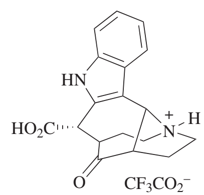
C_{27} 	$(CH_2O)_n$, CSA, DMSO, 70°	 **I** (91)	29, 58
	$(CH_2O)_n$, CSA	**I** +  **II**	29

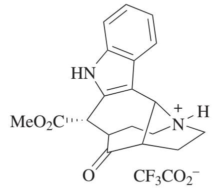
Solvent	Concn (M)	Temp (°)	Time	**I** + **II**	**I**:**II**	
benzene	0.08	80	20 h	(—)	2:1	29
2% aq THF	0.07	65	20 h	(—)	2.7:1	29
DMSO	0.15	73	20 h	(—)	>30:1	29
DMSO	0.05	70	5 d	(91)	100:0	29, 58

TABLE 4. RING-ENLARGING ANNULATION OF AMINO ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27} 	$(CH_2O)_n$, CSA, 80°	 I + II	50, 68

Solvent	Time (h)	I + II	I:II
benzene	22	(>90)[a]	3.5:1
THF	40	(>90)[a]	1:1
$MeNO_2$	18	(>90)[a]	1:13
DMF	18	(72)[b]	1:24
DMSO	23	(75)[b]	1:>30

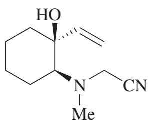
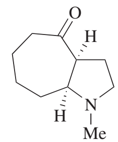
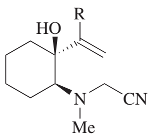
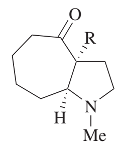
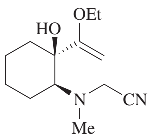
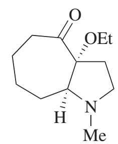
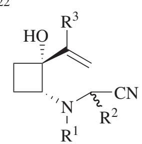
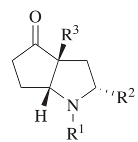
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{30} 	$(CH_2O)_n$, CSA, benzene, reflux, 3–5 h	 (82)	35, 36
C_{31} 	1. TFA, CH_2Cl_2, 0° 2. $(CH_2O)_n$, CSA, benzene, 70° 3. TFA, rt	 (76)	44

	1. TFA, rt 2. $(CH_2O)_n$, MeCN, 70° 3. 0.5 M HCl/MeOH; aq Na_2CO_3, then TFA		(62)	44

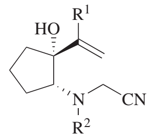
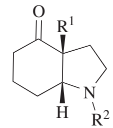
[a] The number is the yield of the crude product.

[b] The number is the yield of the purified product.

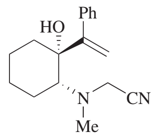
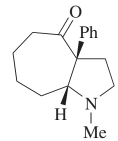
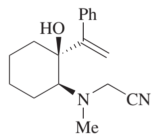
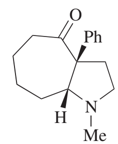
TABLE 5. RING-ENLARGING ANNULATION OF CYANOMETHYLAMINO ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	$AgNO_3$, pyridine, $CHCl_3$, 40°, 19 h	 (64)	25
C_{12-17} 	$AgNO_3$, EtOH, rt, 1 h	 R: Me (78); SPh (76)	25
C_{13} 	$AgOCOCF_3$, ether, rt, 1.5 h	 (37)	25
C_{15-22} 	$AgNO_3$		49

R^1	R^2	R^3	Temp	Time (h)	Yield (%)
Me	H	Ph	50°	4	(78)
Bn	H	H	50°	14	(31)
Me	Me	Ph	60°	0.25	(66)
Bn	H	Me	50°	15	(88)
Bn	H	Ph	50°	2	(93)
Bn	Me	Ph	rt	25	(85)

C_{16} 	$AgNO_3$, ethanol, 1.5 h		29

R^1	R^2	Temp	
Ph	Me	rt	(74)
H	Bn	50°	(40)

C_{17} 	CSA, benzene, reflux, 11 h or $AgNO_3$, ethanol, rt, 1 h	 (60–70)	47
	See table		50

Additive (eq)	Solvent	Temp	Time (h)	
CSA (1.2)	benzene	80°	11	(70)
none	EtOH	80°	11	(—)
$AgOCOCF_3$ (1.1)	$CHCl_3$	rt	1.5	(77)
$AgNO_3$ (1.1)	EtOH	rt	1	(63)
$AgNO_3$ (1.1)/pyridine (13.5)	$CHCl_3$	40°	16	(82)
AgOAc (2.5)	EtOH	rt	23	(76)
$CuOCOCF_3$ (2.8)	$CHCl_3$	rt	1	(91)
$CuOCOCF_3$ (1.2)/Et_3N (1.5)	$CHCl_3$	rt	3.5	(—)

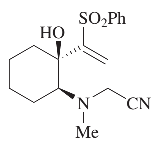
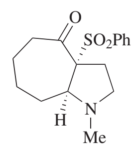
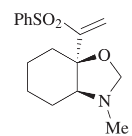
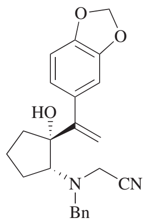
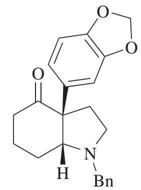
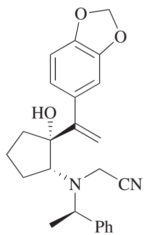
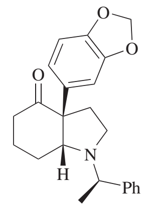
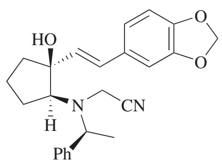
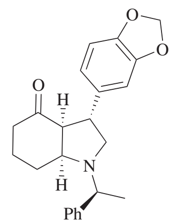
	$AgNO_3$, EtOH, rt, 1 h	 (20) +  (40)	25

TABLE 5. RING-ENLARGING ANNULATION OF CYANOMETHYLAMINO ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{23} 	$AgNO_3$, EtOH, 50°, 2 h	 (94)	29, 47
C_{24} 	$AgNO_3$, EtOH, rt, 3 h	 (80)	48
	1. $AgNO_3$, EtOH 2. BF_3 OEt_2, 5°, 2 h	 (86)	60

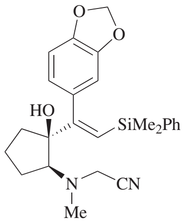
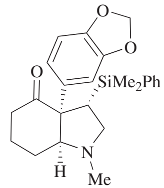
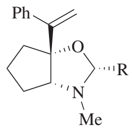
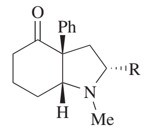
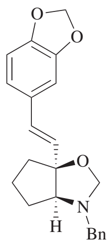
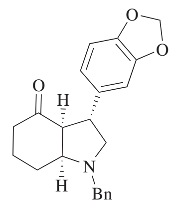
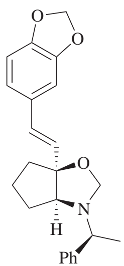
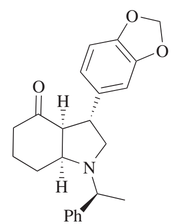
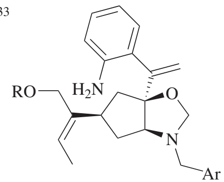
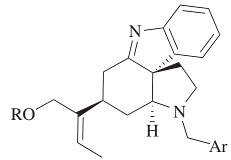
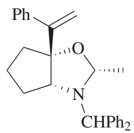
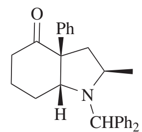
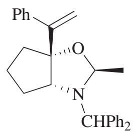
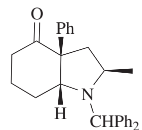
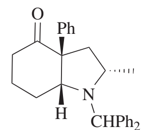
C_{25}		$Cu(OTf)_2$, THF, reflux, 2 h		(94)	46

TABLE 6. RING-ENLARGING ANNULATION OF VINYL OXAZOLIDINES

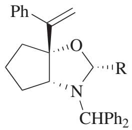
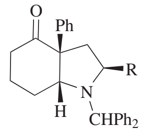
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16-21} 	CSA, MeCN, 60°	 R / Time (h) Me / 24 / (92) *i*-Pr / 24 / (91) *c*-C_6H_{11} / 36 / (91) Ph / 40 / (95)	66
C_{22} 	BF_3•OEt_2, CH_2Cl_2, –20° to rt	 (97)	42, 60
C_{23} 	BF_3•OEt_2, CH_2Cl_2, 5°, 2 h	 (95)	60

Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{25-33} 	CSA, Na_2SO_4, toluene, reflux, 20 min		34
C_{28} 	CSA, CF_3CH_2OH, 60°	 (—)	66
	CSA, 60°	 +  **I** **II**	66

Ar	R	
Ph	H	(51)
Ph	$SiMe_2t$-Bu	(100)
4-$MeOC_6H_4$	Bn	(99)

Solvent	**I + II**	**I:II**
MeCN	(—)	>100:1
CF_3CH_2OH	(—)	2:1

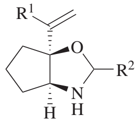
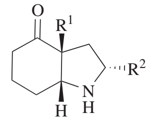
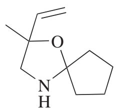
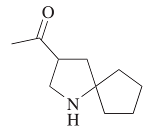
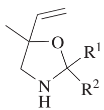
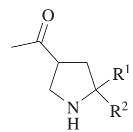
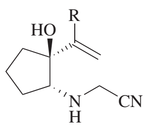
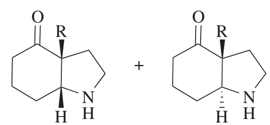
TABLE 6. RING-ENLARGING ANNULATION OF VINYL OXAZOLIDINES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{28-33}			
	CSA, MeCN		66

R	Temp	Time	
Me	60°	40 h	(92)
i-Pr	rt	3 d	(77)[a]
c-C_6H_{11}	rt	12 d	(87)

[a] The conversion was 97%.

TABLE 7. BASE-PROMOTED AZA-COPE/MANNICH REACTIONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-15} 	$Ph_3C^+K^-$ (1.2 eq), THF, rt, 1 h		62
C_{10} 	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt, 24 h	 (66)	61
	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt		61
C_{10-16} 	KH, THF, rt, 14 h		62

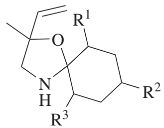
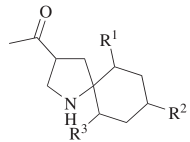
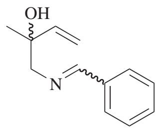
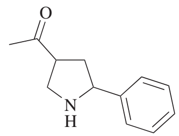
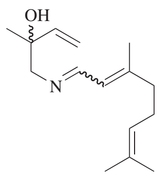
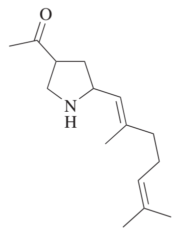
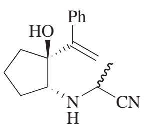
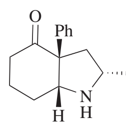
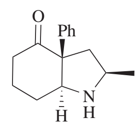
R^1	R^2	
H	H	(68)
Me	H	(72)
Ph	H	(41)
Ph	Me	(80)
3,4-$OCH_2OC_6H_3$	H	(64)

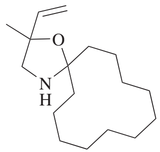
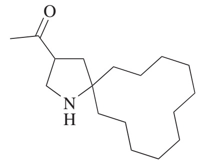
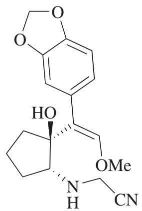
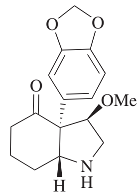
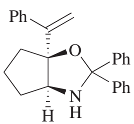
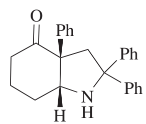
R^1	R^2	Time (h)	
Et	Et	36	(82)
t-Bu	H	24	(72)

I + **II**

R	**I + II**	**I:II**
Me	(74)	3:1
Ph	(54)	>20:1
3,4-$OCH_2OC_6H_3$	(44)	>20:1

TABLE 7. BASE-PROMOTED AZA-COPE/MANNICH REACTIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-15}			
	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt, 24 h	 R^1 / R^2 / R^3 H / H / H (79) Me / H / Me (82) H / *t*-Bu / H (91)	61
C_{12}			
	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt, 24 h	 (91)	61
C_{15}			
	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt, 24 h	 (49)	61
C_{16}			
	KH, THF, rt, 14 h	 (47) +  (24)	62

C_{17} 	KH (1.5 eq), 18-crown-6 (0.1 eq), THF, rt, 24 h	 (84)	61
	KH, THF, rt, 14 h	 (16)	62
C_{26} 	KOH, MeOH, H_2O, reflux, 6 h	 **I** (35)	62
	KH, THF, rt, 42 h	**I** (18)	62

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